Comparative Effectiveness Review
Number 225

Interventions for Substance Use Disorders in Adolescents: A Systematic Review

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This report is based on research conducted by the Brown Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00002-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may periodically be assessed for the currency of conclusions. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at www.effectivehealthcare.ahrq.gov. Search on the title of the report.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see https://effectivehealthcare.ahrq.gov/about/epc/evidence-synthesis.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.
Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Interventions for Substance Use Disorders in Adolescents: A Systematic Review

Structured Abstract

Objectives. This systematic review (SR) synthesizes the literature on behavioral, pharmacologic, and combined interventions for adolescents ages 12 to 20 years with problematic substance use or substance use disorder. We included interventions designed to achieve abstinence, reduce use quantity and frequency, improve functional outcomes, and reduce substance-related harms.

Data sources. We conducted literature searches in MEDLINE, the Cochrane CENTRAL Trials Registry, Embase, CINAHL, and PsycINFO to identify primary studies meeting eligibility criteria through November 1, 2019.

Review methods. Studies were extracted into the Systematic Review Data Repository. We categorized interventions into seven primary intervention components: motivational interviewing (MI), family focused therapy (Fam), cognitive behavioral therapy (CBT), psychoeducation, contingency management (CM), peer group therapy, and intensive case management. We conducted meta-analyses of comparative studies and evaluated the strength of evidence (SoE). The PROSPERO protocol registration number is CRD42018115388.

Results. The literature search yielded 33,272 citations, of which 118 studies were included. Motivational interviewing reduced heavy alcohol use days by 0.7 days/month, alcohol use days by 1.2 days/month, and overall substance use problems by a standardized mean difference of 0.5, compared with treatment as usual. Brief MI did not reduce cannabis use days (net mean difference of 0). Across multiple intensive interventions, Fam was most effective, reducing alcohol use days by 3.5 days/month compared with treatment as usual. No intensive interventions reduced cannabis use days. Pharmacologic treatment of opioid use disorder led to a more than 4 times greater likelihood of abstinence with extended courses (2 to 3 months) of buprenorphine compared to short courses (14 to 28 days).

Conclusions. *Brief interventions*: MI reduces heavy alcohol use (low SoE), alcohol use days (moderate SoE), and substance use–related problems (low SoE) but does not reduce cannabis use days (moderate SoE). *Nonbrief interventions:* Fam may be most effective in reducing alcohol use (low SoE). More research is needed to identify other effective intensive behavioral interventions for alcohol use disorder. Intensive interventions did not appear to decrease cannabis use (low SoE). Some interventions (CBT, CBT+MI, and CBT+MI+CM) were associated with increased cannabis use (low SoE). Both MI and CBT reduce combined alcohol and other drug use (low SoE). Combined CBT+MI reduces illicit drug use (low SoE). Subgroup analyses of interest (male vs. female, racial and ethnic minorities, socioeconomic status, and family characteristics) were sparse, precluding conclusions regarding differential effects. *Pharmacological interventions*: longer courses of buprenorphine (2–3 months) are more effective than shorter courses (14–28 days) to reduce opioid use and achieve abstinence (low SoE). SRs in the college settings support use of brief interventions for students with any use, heavy or problematic use. More research is needed to identify the most effective combinations of behavioral and pharmacologic treatments for opioid, alcohol, and cannabis use disorders.

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Evidence Summary

Main Points

- Adolescents, 12 to 20 years of age, with problematic alcohol and/or cannabis use or use disorder
  - Brief behavioral interventions (that involve 1 or 2 encounters only)
    - Motivational interviewing decreases days of heavy alcohol use and overall alcohol use.
    - Motivational interviewing has not been found to decrease cannabis use. Further research is needed to identify if any other brief interventions may decrease cannabis use.
    - Motivational interviewing decreases problems associated with substance use.
  - Intensive behavioral interventions (that involve more than 2 encounters)
    - Family-focused therapies reduce alcohol use.
    - None of the interventions have been found to decrease cannabis use.
    - Motivational interviewing decreases combined alcohol and other drug use.
    - Combined cognitive behavioral therapy and motivational interviewing decrease illicit drug use.
- Adolescents, 12 to 25 years of age, with substance use disorders
  - Pharmacological interventions
    - In opioid use disorder, longer courses (2–3 months) of buprenorphine/buprenorphine-naloxone are more effective than shorter courses (14–28 days) to reduce days of opioid use and achieve abstinence.
    - More research is needed to understand the role of medications in treatment of alcohol and cannabis use disorders and of pharmacological treatments typically used for comorbid psychiatric illnesses.
- College students with problematic alcohol use
  - Behavioral interventions
    - Mandated alcohol programs decrease alcohol use in the medium term, regardless of intervention. Four commercially available interventions are more effective in the short term than no intervention.
    - Brief behavioral interventions, particularly those based on motivational interviewing, reduce alcohol use compared to no intervention in college students with heavy or hazardous alcohol use.

Background and Purpose

In 2017, an estimated 992,000 adolescents aged 12 to 17 in the United States (4% of the adolescent population) and 5.1 million young adults aged 18 to 25 (14.8% of the young adult population) met diagnostic criteria for a substance use disorder. When left untreated or ineffectively treated, adolescents with substance use disorders are at risk of experiencing a cascade of far-reaching adverse outcomes that often persist into adulthood. The pervasive negative consequences associated with untreated or ineffectively treated adolescent substance use, and the high lethality of opioid misuse, underscore the importance of identifying effective interventions to treat adolescent substance users.

The review aims to inform health care providers, policymakers, and a clinical practice guideline update from the American Academy of Child and Adolescent Psychiatry (AACAP) about the currently available evidence on interventions for adolescents to reduce or cease substance use. The review addresses both behavioral and pharmacological interventions used for adolescents or young adults with problematic substance use or a diagnosis of a substance use disorder (SUD), excluding tobacco.

Methods

We employed methods consistent with those outlined in the AHRQ EPC Program Methods Guidance (https://effectivehealthcare.ahrq.gov/products/cer-methods-guide/overview). We describe these in the full report. Our searches covered reports published from database inception to April 11, 2019. Behavioral interventions were described based on their inclusion of seven primary intervention components: motivational interviewing, family-focused therapy, cognitive behavioral therapy, psychoeducation, contingency management, peer group therapy, and intensive case management. Pharmacologic interventions were divided into those used primarily for problematic substance use (or use disorder) or primarily to manage psychiatric comorbidities. The PROSPERO registration number is CRD42018115388.

Results

We found 118 randomized controlled trials that evaluated treatment of adolescents or young adults with problematic substance use or substance use disorders. Most studies enrolled adolescents with some combination of alcohol and cannabis use. The most commonly reported outcomes included frequency of use and abstinence. We describe evidence about five major categories of interventions: (1) brief behavioral interventions (consisting of one or two encounters), typically targeted at adolescents with problematic use; (2) intensive (nonbrief) behavioral interventions; (3) pharmacological treatments for psychiatric comorbidities in adolescents with concurrent substance use disorder; (4) pharmacological treatments used to treat use disorders; and (5) interventions of any kind for alcohol use in the college setting.

Our meta-analyses of brief interventions found that motivational interviewing reduced heavy alcohol use days by up to 0.7 days per month, alcohol use days by up to 1.2 days per month and overall substance use problems by a standardized mean difference of 0.5, compared to treatment as usual. However, brief motivational interviewing did not reduce cannabis use days (net mean difference of 0).

Of the multiple intensive interventions, family-focused therapies were most effective; they reduced alcohol use days by 3.5 days per month compared to treatment as usual. None of the intensive interventions were found to reduce cannabis use days.

For the subgroups of interest (male versus female, racial and ethnic minorities, socioeconomic status, and family characteristics), data within or between studies of brief and intensive interventions were sparse or not available. Therefore, no conclusions regarding differential effects in these subgroups is possible.

Pharmacologic treatment of opioid use disorder led to a more than 4 times greater likelihood of abstinence with an extended (2 to 3 month) course of buprenorphine compared to short courses (14 to 28 days). Similarly, a slow buprenorphine taper (over 56 days) was more effective than a 28-day taper.

A review of existing systematic reviews found that treatment of problematic alcohol use among college student with behavioral interventions resulted in small improvements in alcohol

use. In students with heavy or hazardous use, single-session interventions resulted in a small reduction in alcohol consumption. In students mandated to treatment, there were small improvements in heavy drinking frequency and alcohol-related problems in the medium term.

Limitations

For many topics, evidence was sparse or entirely absent. Most studies enrolled some combination of adolescents with mixed use of alcohol, cannabis, and occasionally other drugs. Very few studies evaluated users of opioids, methamphetamines, or substances other than alcohol or cannabis. Studies often combined different types of interventions, making comparisons of specific interventions difficult. The available studies did not consistently report a common set of outcomes, which limited our ability to combine information from potentially relevant studies. For most outcomes, individual studies were deemed to have moderate risk of bias, most commonly due to incomplete outcome data, poor compliance, and a lack of blinding of participants, study personnel, and outcome assessors.

The existing systematic reviews addressing treatments for alcohol use in the college setting were inadequate in their assessment and reporting of risk of bias and did not discuss the consistency of results.

Implications and Conclusions

Compared with treatment as usual (e.g., brief advice and a handout), brief motivational interviewing for adolescents with problematic substance use reduces both heavy alcohol use and overall days of use and may decrease problems related to substance use, such as missing school or work or getting into trouble. Among intensive interventions, family therapy (with a focus on intervening in the entire family system) was the most effective in reducing alcohol use.

Neither brief motivational interviewing nor intensive interventions have been demonstrated to reduce cannabis use. For opioid use disorder, buprenorphine and buprenorphine-naloxone are more effective for the short-term management of opioid withdrawal if they are tapered over longer periods of time.

Further research is needed to identify: (1) effective brief and intensive interventions for problematic cannabis use and cannabis use disorder and (2) effective combinations of behavioral treatments and medication to treat alcohol and cannabis use disorder(s). In addition, (3) studies of longer term pharmacological treatment of opioid use disorder are needed in this population. Future studies should evaluate outcomes that are most meaningful to adolescents, such as better functioning in school and improved relationships with peers and parents.

Introduction

Background and Objectives

In 2017, in the United States, an estimated 992,000 adolescents aged 12 to 17 (4% of the adolescent population) and 5.1 million young adults aged 18 to 25 (14.8% of the young adult population) met diagnostic criteria for a substance use disorder (SUD).[1] Thus, about 1 in 25 adolescents and 1 in 7 young adults had a diagnosable SUD. The vast majority were untreated, with fewer than 1 in 10 adolescents or young adults with a diagnosable condition receiving specialty care.[1] When left untreated or ineffectively treated, adolescents with problematic substance use are at risk of experiencing a cascade of far-reaching adverse outcomes that often persist into adulthood, including sexually transmitted infections,[2] unintended pregnancy,[3] criminal involvement,[4] school truancy,[5] psychiatric disorders,[6] and physical health problems.[7] Adolescent substance use is also associated with the leading causes of death in this age cohort: suicide, unintentional injury, and violence.[8, 9]

Alcohol, marijuana, and tobacco are the most commonly misused substances, followed by prescription and over-the-counter medications, among twelfth graders;[10] with 1 percent of youth between the ages of 12 and 17 reporting current opioid misuse.[11] Youth who use opioids are more likely to use other substances.[10] Among youth under 21 who initiate heroin use, 80 percent misused prescription and/or over-the-counter medication before the age of 18.[12] National concerns about opioid misuse, encompassing nonmedical use of prescription opioid-based medications (e.g., morphine, fentanyl) and the use of illegal opiates (e.g., heroin), have brought heightened attention to the significant risk of drug overdose death in adolescents.[13]

The pervasive negative consequences associated with untreated or ineffectively treated adolescent substance use (SU), and the high lethality of opioid misuse in particular, underscore the importance of identifying effective interventions for substance use in adolescents.

In 2005, the American Academy of Child and Adolescent Psychiatry (AACAP) created a Practice Parameter (PP) for the Assessment and Treatment of Children and Adolescents with substance use disorders. The 2005 Practice Parameters made eight recommendations pertaining to treatment. For behavioral treatments, AACAP concluded that family therapy models "have the most supporting evidence" and "individual approaches such as cognitive-behavioral therapy, both alone and with motivational enhancement therapy, have been shown to be efficacious." AACAP recommended that "medication can be used when indicated," noting that this recommendation was "not based on empirical research in adolescents but rather on research and experience with adults."[14] The AACAP also recommended that psychiatrists consider co-occurring mental health disorders, since the majority of adolescents with substance use problems present with a co-occurring mental health diagnosis. Recommendations made in the 2005 PP were limited by a relative lack of rigorous trials at the time.

Since the publication of the 2005 PP, there has been a proliferation of adolescent substance use treatment trials, many of which have employed more rigorous designs, larger samples, random assignment, direct comparisons of two or more active treatments, improved measures of substance use and other variables, newer interventions (e.g., manual-guided interventions), and longer-term outcome assessments. This systematic review (SR) will inform a Clinical Update and Clinical Practice Guideline to update the 2005 AACAP PP for the Assessment and Treatment of Children and Adolescents with SUDs. Given the high co-occurrence of substance use and other mental illnesses, and the increased focus on integrated treatment, there is a great \

need to evaluate the evidence, and to engage researchers and clinicians, including primary care physicians, regarding the most effect treatments for substance use in adolescents.[15]

In 2014, a guide developed by the National Institute of Drug Abuse (NIDA) identified multiple approaches to treating adolescent SUDs, which were divided into behavioral approaches, family-based approaches, addiction medicine, and recovery support services, but this report did not synthesize evidence on comparative effectiveness.[16] The American Academy of Pediatrics (AAP) Committee on Substance Use and Prevention recently recommended consideration of pharmacotherapy for adolescent and young adult patients with severe opioid use disorders or co-occurring alcohol use disorders.[17] Thus, there is a significant need for a rigorous and comprehensive synthesis of the adolescent substance use treatment literature that addresses both pharmacologic and psychological treatments.

The overarching goal of this review is to evaluate the available evidence for the treatment effects (and comparative effects) of available behavioral and pharmacologic interventions to manage SUD and problematic use (not including tobacco) in adolescents and young adults. The review evaluates treatment effects across population subgroups and identifies evidence (or gaps in evidence) regarding the key ingredients of successful interventions for problematic substance use in adolescents and young adults. For most specific topics, we conducted *de novo* systematic review, but for treatment of alcohol use disorders/problematic alcohol use in the college setting, we summarized existing SRs, since this literature is large, highly contextual, and has been extensively reviewed.

Key Questions

Key Question 1. What are the effects of behavioral, pharmacologic, and combined interventions compared with placebo or no active treatment for substance use disorders and problematic substance use in adolescents to achieve abstinence, reduce quantity and frequency of use, improve functional outcomes, and reduce substance-related harms?

a. How do benefits and adverse outcomes of interventions vary by subpopulations?

b. How do benefits and adverse outcomes of interventions vary by intervention characteristics

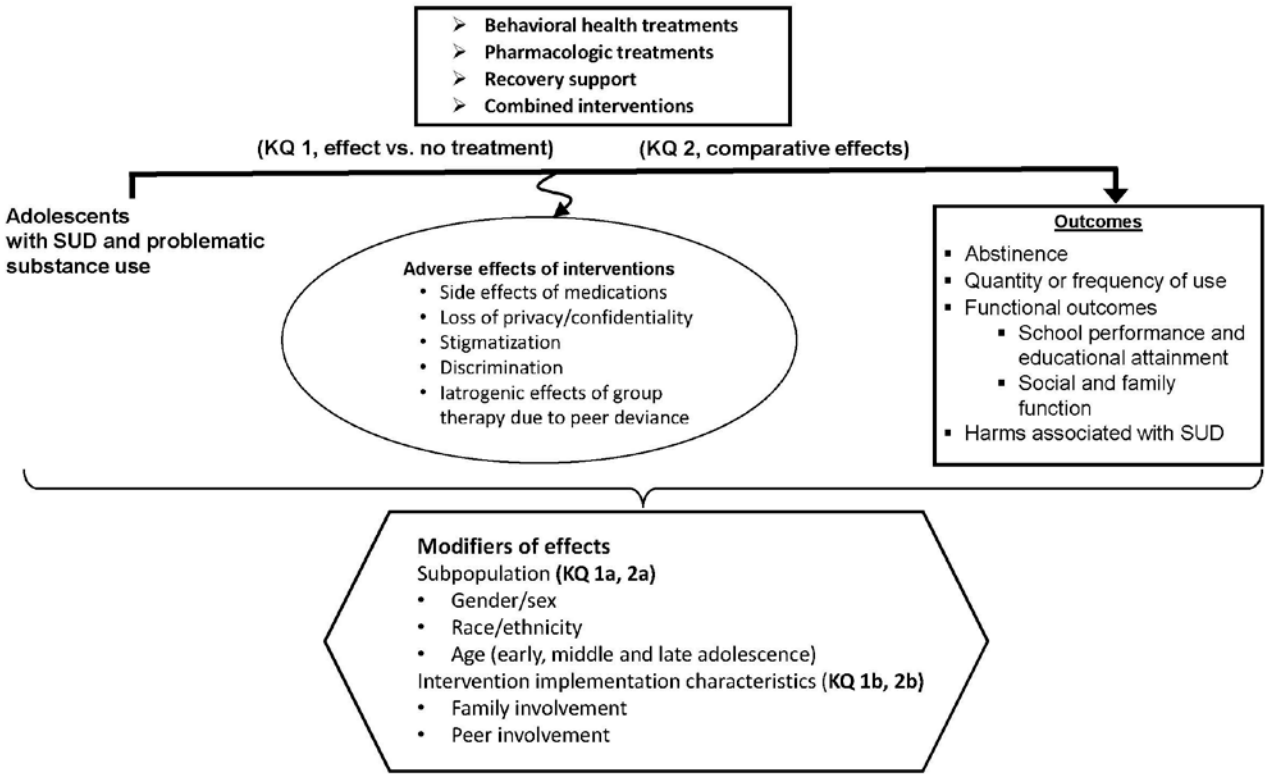
Key Question 2. What are the comparative effects of active interventions for substance use disorders and problematic substance use in adolescents to achieve abstinence, reduce quantity and frequency of use, improve functional outcomes, and reduce harms?

a. How do comparative benefits and adverse outcomes of interventions vary by subpopulations?

b. How do comparative benefits and adverse outcomes of interventions vary by intervention characteristics?

The analytic framework for the key questions is shown in Figure 1.

Figure 1. Analytic framework for the Key Questions



Methods

The Evidence-based Practice Center conducted the review based on a systematic review (SR) of the scientific literature, using established methodologies as outlined in the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[18] The PROSPERO registration number is CRD42018115388.

Searching for the Evidence

We conducted literature searches in MEDLINE, the Cochrane CENTRAL Trials Registry, Embase, CINAHL, and PsycINFO databases (all from inception) to identify primary studies meeting our criteria through April 11, 2019. As a part of an independent methods project, an interim search of MEDLINE was undertaken using text mining tools on October 30, 2018. A separate search for SRs of interventions for alcohol disorders/problematic alcohol use in the college setting was conducted in MEDLINE, Cochrane Database of Systematic Reviews, and Epistemonikos also through April 11, 2019; after discussion with the Technical Expert Panel (TEP), it was decided to restrict the review of this topic to existing SRs because the literature is vast and has been extensively reviewed. All search strategies are detailed in Appendix A. The search strategies were peer reviewed by an independent, experienced information specialist/librarian. We asked the TEP to provide citations of potentially relevant articles. We also perused the reference lists of published clinical practice guidelines and relevant existing SRs for eligible studies. We also searched ClinicalTrials.gov on October 30, 2018 to identify unpublished and ongoing studies, and the U.S. Food and Drug Administration (FDA) Web site on October 30, 2018 for pharmacologic trials.

Peer and public review provided an additional opportunity for the TEP and other experts in the field to ensure that no key publications were missed. Finally, a Supplemental Evidence and Data for Systematic review (SEADS) portal and Federal Register Notice was posted for this review.

Study Eligibility

Table 1 and the following paragraphs detail the eligibility criteria.

Population

Adolescents

We included studies of adolescents and young adults. Our *a priori* definition of this population's age range was 12 to 20 years inclusive. Our search was designed to identify studies whose lower inclusion ages overlapped our age range of interest. Thus, we screened the full text of otherwise eligible studies that also included transition age youth (age 21 to 25) and adults (age 18 and above) for reported subgroups. For studies of behavioral interventions, we excluded studies that enrolled more than 20 percent of subjects older than our *a priori* upper age of 20 years. Because of the relative sparseness of studies of pharmacologic interventions, we expanded the upper inclusion age to 25 years inclusive.

Substance Use-Related Eligibility Criteria

We included studies that enrolled patients with substance use disorder(s) or problematic use of all substances except for tobacco.

We included studies that enrolled participants with at least one substance use disorder diagnosis, or subjects with problematic use.

Substance Use Disorder

Studies were considered to have enrolled subjects with substance use disorder if subjects met DSM-III, DSM-IV or DSM-V criteria for one or more substance use disorders (except tobacco).[19-21]

Problematic Use

A designation of problematic use was applied if a study applied one or more of the following inclusion criteria: (1) subjects were referred for treatment by self, parent, school, other professional, or the juvenile justice system; (2) subjects were screened using a validated tool, such as the AUDIT-C (Alcohol Use Disorders Identification Test—Consumption)[22] and an intervention was given to those who met a prespecified threshold; (3) subjects were asked about amount and frequency of use, and a threshold of at least monthly substance use was defined or; (4) subjects were identified after a consequence of substance use, such as an alcohol related emergency department visit.

Interventions and Comparators

Each study of behavioral interventions was categorized as either brief (if the intervention consisted of one or two sessions), or nonbrief (defined as 3 or more sessions). The broad range of behavioral interventions were consolidated into combinations of seven primary intervention components and four intervention modifiers, based on components identified in prior SRs (see *Intervention Coding* below for details).

Two distinct categories of pharmacologic interventions were considered: (1) medications used specifically to reduce and/or eliminate substance use and to prevent relapse, and (2) medications to treat co-occurring psychiatric disorders in patients with concurrent problematic substance use or substance use disorder. The latter set of medications were considered substance use treatments only if their effects on substance use were explicitly examined.

Outcomes

Use-related outcomes for specific substances (e.g., alcohol, cannabis) and outcomes that aggregated multiple substances were eligible for synthesis. We extracted continuous measures reflecting frequency of use and categorical measures of abstinence. For alcohol, we considered both frequency of heavy alcohol use (e.g., mean days of heavy use per 30 days) and frequency of any use (e.g., percent days of alcohol use per 30 days).

Aggregate outcomes of use or abstinence for multiple substances were classified into one of three categories: (1) *alcohol and other drugs*, (2) *illicit drug use* (excludes alcohol, but includes cannabis and other drugs, regardless of local laws), (3) *other drugs* (which explicitly excludes alcohol and cannabis).

A variety of substance use related problem scales were encountered, and they are detailed in Appendix H. When a study reported multiple problem scales that reflected problems associated with use of a specific substance, we chose the scale with the highest mean severity in each study.

Study Designs

For studies of behavioral interventions and of pharmacologic treatment of psychiatric comorbidities, we included only randomized controlled trials with a minimum of 10 patients per arm.

For pharmacologic interventions of medications specifically to reduce and/or eliminate substance use and to prevent relapse, we included randomized controlled trials with a minimum of 10 patients per arm, and nonrandomized comparative studies or single group studies enrolling at least 100 patients per arm.

Table 1. Eligibility criteria

PICOTS	Inclusion	Exclusion
Population	Adolescents • Nonpharmacologic (12 – 20 years, inclusive) • Pharmacologic (12 – 25 years, inclusive) Substance use disorder or problematic use of: • Alcohol • Cannabis • Opioids, including nonmedical prescription and illicit • Sedatives, hypnotics, or anxiolytics • Stimulants, including nonmedical prescription and illicit • Inhalants • Hallucinogens • Unspecified or polysubstance use *Subpopulations of particular interest* • *Psychiatric comorbidities* • *Age subgroups (12-14, 15-17, 18-20 years)* • *Sex, gender, and sexuality* o *Male/female, cis/transgender, orientation* • *Racial/ethnic minority* o *White* o *African American/Other* o *Hispanic* • *Socioeconomic status and related characteristics* • *Pregnancy, postpartum, parenting* • *Family characteristics* o *Demographics, family dynamics, involvement with child protection services*	For nonpharmacologic studies, if >20% of study sample (or identifiable subgroup) is <12 or > 20 years, combined For pharmacologic studies, if >20% of study sample (or identifiable subgroup) is <12 or >25 years, combined Tobacco/nicotine use (including if the polysubstance use is predominantly tobacco/nicotine) Substance use not meeting definition of at least "problematic use"

PICOTS	Inclusion	Exclusion

Interventions	Behavioral health treatments
	• Family therapies
	  ○ Family behavioral therapy, family systems therapy, brief strategic family therapy, functional family therapy, ecological family therapy, multidimensional family therapy, family systems network, educational family therapy, multisystemic therapy, others
	• Cognitive behavioral therapy
	  ○ Adolescent community reinforcement approach, dialectical behavioral therapy, cognitive therapy, others
	• Contingency management
	• Motivational interviewing or enhancement therapy
	• Psychoeducation (aimed at substance use)
	• Recovery support
	  ○ 12-step programs, peer-based and/or peer supports, assertive continuing care, others
	• Other (e.g., culturally sensitive interventions)
	• Multicomponent interventions (2 or more models)
	• Integrated interventions (for substance use and a co-occurring disorder)
	  • *Behavioral interventions are divided by duration*
	  ○ *Brief interventions (1 or 2 sessions only)*
	  ○ *Nonbrief interventions (≥3 sessions)*
	Pharmacologic interventions
	• Medications used specifically to reduce and/or eliminate substance use and to prevent relapse
	  ○ For alcohol
	  ▪ Gabapentin, naltrexone, acamprosate, disulfiram, topiramate, ondansetron
	  ○ For cannabis
	  ▪ N-acetylcysteine
	  ○ For opioids
	  ▪ Methadone, buprenorphine, combination buprenorphine and naloxone, naltrexone
	• Medications to treat co-occurring psychiatric disorders in patients with concurrent problematic substance use or substance use disorder (regardless of primary goal of treatment with the drug)
		Preventive interventions (i.e., interventions among nonusers to prevent future substance use)
		Interventions not aimed at reducing substance use (e.g., needle exchange, condom promotion)
		Medications to treat overdose
		Pharmacologic management of acute withdrawal symptoms

Comparators	Key Question 1 • No active treatment, including waitlist and placebo • Treatment as usual (including if poorly defined) • Education or other materials (not aimed at substance use) Key Question 2 • Any other active intervention, including interventions both within a given category (e.g., comparing two types of cognitive behavioral interventions)	For Key Question 2, within-category comparisons, if differ only in personnel (e.g., years of therapist training)

PICOTS	Inclusion	Exclusion
Outcomes	Use outcomes • Frequency of use (self report) o Days of use over specified time period o Heavy alcohol use days over specified time • Abstinence (objective or self-reported) • Severity of use o Substance-related problems or symptoms counts or scales Functional outcomes • School performance and educational attainment, including attendance, academic performance, graduation, entering higher education, and others • Social relationships, including family functioning, peer relationships, and others Harmful consequences of substance use • Serious mental health events, including suicidal ideation and behavior • Physical health, including mortality, substance-use-related morbidities, infections (e.g., HIV, hepatitis C, other sexually transmitted diseases) • Serious legal events, including arrest, recidivism, contact with juvenile justice system Adverse events of interventions • Side effects of pharmacologic interventions • Loss of privacy or confidentiality • Stigmatization or discrimination • Iatrogenic effects of group therapy due to peer deviance • Other reported adverse effects ascribed to interventions	None
Timing	Minimum 1 month followup (since the start of the intervention)	None
Settings	Any, including community, residential, jail/prison, court-mandated, etc. Any country or geographic area	College setting (for alcohol)*
Study designs	All studies: • Published, peer-reviewed articles or unpublished data from the FDA or from the Results reported on ClinicalTrials.gov web site • Any publication date *For any intervention and outcome (except alcohol use among college students)*: • Randomized controlled trials • N≥10 per study group *For pharmacologic studies reporting adverse events, as above and*: • Nonrandomized comparative studies, prospective or retrospective, N≥100 per study group • Single group, prospective or retrospective, N≥200 *For studies of alcohol use among college students*: • Systematic reviews of randomized controlled trials	Case control studies Cross-sectional studies Case reports or series
Publication language	Any	Unable to read, translate, or retrieve

Abbreviations: FDA = Food and Drug Administration; N = sample size; PICOTS = populations, interventions, comparators, outcomes, timing, setting

*Because we did a review of reviews for alcohol in the college setting, we excluded primary studies thereof.

Screening Studies for Eligibility

For citation screening, we initially conducted a series of pilot training sessions to achieve a satisfactory level of agreement among researchers regarding the nuances of the eligibility criteria for title and abstract screening. Because abstracts sometimes do not mention all outcomes that are reported in the full-text, we did not exclude titles and abstracts based on outcomes. We conducted all abstract screening using the open-source, online software Abstrackr (http://abstrackr.cebm.brown.edu/). To assist with screening, we used the predictive algorithm capabilities of Abstrackr, which frontloads more-likely-to-be-relevant citations. We began with double, independent screening of abstracts. Conflicts were resolved during full-group meetings. Using the labels (accept, reject) given to screened abstracts, Abstrackr determines a prediction value for all remaining unscreened citations and sorts these such that the most-likely-to-be-accepted abstracts are screened first. Based on empirical research on Abstrackr (soon to be submitted for publication), when all remaining unscreened abstracts have a prediction value <0.40 (on a scale of 0 to 1), these abstracts are highly likely (>99% probability) to be rejected. We, thus, double screened abstracts until this threshold was met; thereafter, we switched to single screening of remaining abstracts.

We obtained the full-texts of all citations that were screened in (accepted) during abstract screening. The reference lists from SRs were reviewed for the presence of additional primary studies. We evaluated these articles using an evidence map structure, in which we gathered basic data on each article (i.e., study design, sample size, confirmation of substance use disorder/problematic use, age data, intervention(s), confirmation of outcomes of interest). Articles derived from the same studies (multiple publications, secondary analyses) were grouped. Using this process, we determined final eligibility status for each study.

Data Extraction

Studies with multiple publications or secondary analyses were extracted as one study. Multiple studies reported in a single publication were extracted separately. Small teams of researchers focused on extraction of different elements from each of the studies. One team extracted study design, population characteristics, and baseline data; one team extracted and categorized interventions (as described in the next section); one team extracted outcome descriptions and study results; one team extracted risk of bias information. Each section of each study was extracted by one researcher and then verified by at least one other experienced researcher. Discrepancies were discussed between them, as needed.

Data were extracted into customized forms in the Systematic Review Data Repository (SRDR) online system (http://srdr.ahrq.gov) or into separate spreadsheets designed to capture all elements relevant to the Key Questions (KQs). Upon completion of the review, all data were uploaded to SRDR, and the SRDR database was made accessible to the public, with capacity to read, download, and comment on data.

The basic elements and design of these forms are similar to those we have used for other comparative effectiveness reviews and include elements that address population characteristics; descriptions of the interventions and comparators; outcome definitions; intervention modifiers; sample sizes; study design features; funding source; results; and risk of bias.

We did not contact study authors for additional data.

Intervention Coding

Each active intervention was categorized as either a brief (defined as 1 or 2 sessions) or nonbrief (defined as 3 or more sessions) intervention. To be classified as a "session" the adolescent had to connect directly with a therapy provider either in-person, by phone, or on the Web. Text message prompts or queries were not considered sessions.

A codebook (Appendix C) with definitions for seven primary intervention components and intervention modifiers was developed by the Scientific Lead based on the most commonly reported approaches in prior SRs.[23-25] The intervention components were:

- Motivational interviewing (MI)
- Family focused therapy (Fam)
- Cognitive behavioral therapy (CBT)
- Psychoeducation (Educ)
- Contingency management (CM)
- Peer group therapy (PeerGroup)
- Intensive case management (ICM).

Each study was independently coded by two investigators, one with expertise in adolescent substance use interventions and the other with expertise in the analysis of multi-component health service and behavior interventions. After assigning one or more intervention components to each study arm, the investigators reviewed and compared intervention codes and identified discrepant codes, which were discussed in detail with the goal of obtaining consensus. In cases when discrepancies were not resolved via discussion, a third senior investigator with expertise in adolescent substance use interventions reviewed the codes and served as the tie breaker.

The coders assigned four intervention modifiers: delivery of therapy in groups, additional parent involvement, culturally accommodated treatment, and integrated interventions targeting both substance use and mental health. The definitions for the intervention components and modifiers are described below.

General Principles

The following principles guided intervention coding:

a. Intervention components had to be unique and distinct from one another (e.g., if a CBT intervention described educating adolescents about skills, we did not code education unless there was a distinct psychoeducational session or module);
b. Intervention components had to be sufficiently well described to ensure that all adolescents consistently received the treatment (e.g., if usual services was referral to an intervention or host of potential interventions but was not standardized to ensure all adolescents received it, we did not code the presence of the intervention component). Related, vaguely described intervention components lacking reference to a specific manual or another form of fidelity monitoring were not coded as having a component (e.g., intervention described as "motivational interviewing informed" or "cognitive behavioral therapy inspired"); and
c. Study arms that were reported as "treatment as usual" (TAU) were coded as having specific intervention components if the description treatment met the definition of the components and threshold criteria above.

Motivational Interviewing (MI)

We coded an intervention as containing MI if it explicitly described at least one session focused on building the adolescent's motivation to reduce substance use and/or attain abstinence. Motivation enhancement therapy (MET), a more structured and specific approach to building the adolescent's motivation, was also categorized as MI. MET typically includes techniques, such as a decisional balance and personalized feedback on substance use patterns with normative comparisons, which are specifically designed to enhance motivation to change.

Family, cognitive behavioral, and educational therapy models that generally referenced a goal to build the adolescent's motivation to change were not coded as containing MI unless there was a stand-alone, manual-guided intervention MI component. If MI was delivered to the parent either instead of or in addition to the adolescent sessions, this was recorded and assigned a parent involvement qualifier.

Family Therapy (Fam)

We coded an intervention as containing family therapy if sessions were predominantly delivered with the entire family present and if the focus of the therapy was on changing the adolescent's substance use by intervening with the entire family system. Interventions that were delivered predominantly to the adolescent and that contained parent-only sessions or periodic family check-ins were not categorized as family therapy. Building upon the classifications used in prior SRs (Becker & Curry, 2008; Hogue et al., 2018),[26, 27] we assigned qualitative descriptors to describe family therapy models within five broad categories: ecological, systems/structural, behavioral, functional, and educational. These categories were assigned to enhance the qualitative description of distinct models but were not included in the quantitative synthesis.

Ecological models explicitly targeted adolescent substance use in the context of extrafamilial influences across multiple interrelated, nested systems. Example intervention models included multidimensional family therapy, ecological family therapy, and multisystemic therapy.

Systems/structural approaches attempted to restructure problematic family interaction patterns associated with the adolescent's substance use. Systems/structural models included brief strategic family therapy, family systems therapy, and family structural therapy.

Behavioral approaches were those that applied principles of operant conditioning and social learning within the family context in order to encourage healthy behavior and discourage substance use.

Functional approaches integrated principles of both systems and behavioral approaches, such as functional family therapy.

Educational approaches explicitly aimed to address the adolescent's substance use through the provision of psychoeducation to the entire family.

Cognitive Behavioral Therapy (CBT)

We coded an intervention as containing CBT if it explicitly described using a manual or protocol focused on providing the adolescent with either cognitive (e.g., thought identification, thought modification) or behavioral (e.g., peer refusal, communication, problem solving) skills needed to reduce substance use and/or attain abstinence. CBT was only coded in adolescent-focused intervention components: family models that focused on building skills to change were coded as family behavioral therapy. Because all CBT models involve some degree of parent involvement, an intervention was coded as CBT if sessions were primarily delivered to the

adolescent alone (even if there were some parental involvement in the form of updates, parent only sessions, or parent check-ins) and categorized as family behavioral therapy if sessions were primarily delivered to the entire family.

Peer Group Therapy (PeerGroup)

Adolescent peer group therapy models were nondirective therapy interventions delivered to adolescents in group format, which aimed to reduce the adolescent's substance use by having adolescents interact and provide social support. Interventions were coded as containing adolescent peer group therapy if the following two conditions were met: a) clear reference to therapy sessions delivered to adolescents in group format; and b) sessions were described as interactive, process-oriented, and/or following a self-help approach. Group therapy sessions that explicitly referenced a CBT or psychoeducational manual were not coded as peer group therapy: such approaches were coded as CBT or psychoeducation, respectively, and assigned the group therapy intervention modifier.

Psychoeducation (Educ)

Psychoeducational interventions were interventions explicitly designed to reduce the adolescent's substance use through the provision of education about the harms of alcohol and illicit drugs. An intervention was coded as containing psychoeducation if it had an explicit stand-alone module focused on the provision of education. Because the majority of intervention models designed for the target population involve some degree of education about adolescent substance use, we only coded an intervention as containing psychoeducation if there was explicit reference to a stand-alone psychoeducation module or intervention. For example, family therapy, MI, and CBT models that made general reference to providing education to parents or teens were not coded as educational unless they had a clearly specified independent psychoeducation component.

Contingency Management (CM)

CM interventions explicitly described the provision of external, consistent reinforcement for the adolescent's attainment of pre-defined goals. An intervention was coded as containing CM if it described a specific protocol (e.g., manual, prize schedule) for positive reinforcement of the adolescent's behavior. Family therapy models that taught the parent how to monitor and reinforce the adolescent's behavior through household contracts were not coded as containing CM unless the reinforcement was explicitly provided as a part of the therapy sessions: intervention approaches in which parents learned to provide reinforcement were coded as CBT or family behavior therapy. Additionally, we only coded an intervention as CM if the reinforcement was positive in nature: enforcement of negative consequences for missed sessions or positive urine screens (e.g., as part of family or drug court) were not considered CM.

Intensive Case Management (ICM)

Intensive case management interventions were interventions in which the primary focus was on linking the adolescent to supportive services. Interventions were coded as intensive case management if they identified specific protocols focused on promoting continuity of care (e.g. assertive continuing care).

Treatment as Usual (TAU)

Interventions designed to be comparators to active intervention and were not directed at treating substance use were categorized as TAU. Examples included waitlists or pamphlets regarding issues other than substance use. In addition, interventions that were not adequately described, actively monitored for fidelity, or in which it was not possible to determine whether all adolescents received the same intervention, were coded as TAU.

Intervention Modifiers

In addition to coding primary intervention components, we coded several intervention modifiers, as follows:

Group involvement. Therapy models were coded as group if any of the intervention elements were delivered in group format. This modifier encompassed a broader range of studies than the peer group therapy code. Studies that described parent-only groups and family groups were captured by this effect modifier, as were studies that described manual-driven CBT delivered in a group format or psychoeducational group therapy.

Parent Involvement. Nonfamily models were coded as having substantial parent involvement if they specifically described delivering intervention elements to parents only (i.e., parent-focused intervention) or if they described frequent parent check-ins.

Culturally accommodated. Therapy models that were specifically designed as adaptations for specific cultural groups were classified as culturally accommodated. Models had to explicitly reference being adapted for specific cultural groups or using formative work with specific cultural populations to receive this designation.

Integrated interventions. Interventions that were specifically designed to target co-occurring substance use and mental health diagnoses were coded as integrated. This modifier was only coded if the intervention was explicitly designed to address dual substance use and mental health diagnoses. If the sample had high proportions of dual diagnosis patients, but the intervention did not specify a specific focus on diagnoses of interest, then this modifier was not coded. Similarly, if the intervention targeted substance use and a co-occurring physical health concern such as HIV or sexual risk, then this modifier was not coded.

Assessment of Risk of Bias

Two senior investigators, highly experienced in SR and risk of bias assessment, assessed the risk of bias for all studies. After two rounds of double, independent risk of bias assessment, with adjudication of 10 studies per round, the remaining studies were assessed by one investigator and verified by the other (each was the primary assessor for about half the studies).

We assessed the risk of bias (methodological quality) of each study based on predefined criteria. For all studies, we used the Cochrane risk of bias tool,[28] which examines methodological items, such as random sequence generation; allocation concealment; blinding of participants, care providers, and outcome assessors; incomplete outcome data; and selective reporting, to inform judgments about various sources of bias and overall risk of bias assessments. We also assessed whether intention-to-treat analyses were conducted. In addition, we used relevant questions from the Newcastle Ottawa Scale,[29] including similarity of groups at baseline, whether any cointerventions differed between groups, absolute and comparative compliance, timing of outcome assessments (between groups), and any additional biases.

If a randomized trial used an "urn method" for randomization (used to balance groups among prespecified participant characteristics) we assumed that randomization method and allocation concealment were low risk of bias (since randomization would need to be done centrally by computer). For outcome assessor blinding of nonpharmaceutical interventions, we assessed whether the outcome assessors were blinded to intervention group; if so, we determined these studies were low risk of bias for outcome assessor blinding (even though the adolescent users reporting substance use to the outcome assessor may not have been blinded). For incomplete outcome data (attrition bias) and compliance, we deemed studies to be high risk of bias if more than 20 percent of participants dropped out or did not comply with the intervention, regardless of whether intention-to-treat analyses were conducted. Regarding selective outcome reporting, we captured information from available protocols (including from ClinicalTrials.gov) on planned outcomes. For group similarity, we captured information about the statistical significance of differences between groups at baseline; if there were differences, but these were statistically accounted for in analyses, we deemed these to be low risk of bias.

For SRs of interventions for alcohol use disorder or problematic alcohol use in the college setting, we assessed SR quality using specific items from AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews, version 2).[30] We omitted questions about SR protocol timing, justification of excluded studies, study funding sources, and assessment of publication bias. Also, two questions about description of eligibility criteria were combined as were two questions about assessment of risk of bias in their analyses were combined. Thus, the risk of bias questions (with corresponding item numbers in AMSTAR 2) included: description of eligibility criteria (item 1), comprehensive search strategy (item 4), duplicate study screening (item 5), duplicate data extraction (or with verification) (item 6), adequate description of details of included studies (item 8), use of a satisfactory technique for assessing risk of bias in included studies (item 9), appropriate meta-analysis methods (if applicable) (item 11), assessment of potential impact of risk of bias (item 12), explanation and discussion of any heterogeneity (item 14), and reporting of SR conflict of interest (item 16). We deemed that SRs that meta-analyzed (standardized) "effect sizes" across disparate outcomes did not address the KQs of our systematic review because they indiscriminately combined highly heterogeneous outcomes. Furthermore, some SRs included multiple outcomes from the same underlying trials without correction for correlation or for double-counting.

For all studies, any quality issues pertinent to specific outcomes within a study were noted and applied to those outcomes. Quality issues pertinent to specific outcomes within a study were noted and considered when determining the overall strength of evidence (SoE) for conclusions related to those outcomes.

Detailed risk of bias assessments for each study are listed in Appendix H. A summary of the risk of bias for the studies in each group eligible for meta-analysis is displayed in a stacked bar chart.

Data Synthesis

Frequency of use outcomes were reported in multiple forms. If use was reported as days of use per time interval (e.g., days of use per month, percent use days per 90 days), mean use was converted to a common metric of mean use days per 30 days, despite the acknowledged caveat that this metric assumes that use was constant over the various reporting intervals.

We preferentially included outcomes evaluated at 4 months after baseline assessment. If outcomes were not reported at 4 months, we accepted the closest followup time in the range from

1 to 6 months (in the case of ties, e.g. data available for both 3 months and 5 months, we chose the earlier time). Abstinence outcomes were summarized as odds ratios.

For continuous outcomes with an available baseline data scale, we evaluated the "net mean difference" (NMD) of the outcome, the difference between arms of the within-arm changes in outcome.

When necessary, standard errors (SE) of the differences were estimated from reported standard deviations (or SEs) of baseline and final values. For parallel trials, we assumed a correlation of 0.5 between baseline and final values in patients receiving a given intervention. Thus, we used the following equation to estimate the SE:

$$SE^2_{difference} = (SE_A)^2 + (SE_B)^2 - 2 \cdot r \cdot (SE_A) \cdot (SE_B)$$

where r=0.5 (the assumed correlation) and A and B index the correlated measurements (baseline and final time points).

Standardized net mean differences (SNMD) were calculated for substance use problem scales. In a sensitivity analysis, we calculated standardized net mean differences (SNMD) to enable combined analyses of: 1) scales that reflected (intensity of) substance use, and 2) nonlinear transformations, e.g. square root of mean use days, and substance specific days of use outcomes.

A minority of studies did not report either standard continuous or categorical outcome metrics, but instead either summarized models with metrics that could not be converted to net difference, odds ratio, or risk ratio, or reported only statistical significance (with or without directionality). These were not included in the quantitative analysis and are not explicitly summarized in the review text. Their results are included in the Evidence Tables and, electronically, in the SRDR project file.

Qualitative Evidence Synthesis

Prior to meta-analysis, with input from subject matter experts, we qualitatively evaluated whether populations were sufficiently comparable for quantitative synthesis.

We assessed population comparability in two ways. First, we identified the study inclusion criteria to determine whether each study targeted alcohol, cannabis, another drug, or a combination of substances. Next, we assessed substance use reported in the recruited samples. Although study eligibility criteria were heterogeneous in terms of targeted substances; the final samples were predominantly comprised of adolescents with some combination of alcohol and cannabis use, with a minority using other drugs. Studies that specified substances other than alcohol and cannabis in their eligibility criteria (e.g. ecstasy or cocaine,[31] methamphetamine,[32] inhalants[33]) were excluded from meta-analyses.

The vast majority of studies reported overlapping substance specific outcomes (i.e., a given study might report cannabis outcomes, alcohol outcomes or both). We analyzed these outcomes separately by substance. Thus, a given study might contribute to a cannabis analysis, to an alcohol analysis, or to both. Some studies only reported an aggregate use measure, e.g., alcohol and other drug use or illicit drug use.

Substance use problem scales were combined and pooled across substances.

Quantitative Evidence Synthesis

We conducted pairwise meta-analyses (MA) using both frequentist and Bayesian frameworks, and network meta-analyses (NMA) in the Bayesian framework. Analyses were done using R,[34] with the *metafor*[35] and *gemtc* packages.[36]

MAs used a random effects model assuming that within-study estimates and between studies true effects are normally distributed.

NMA is an extension of pairwise meta-analyses that simultaneously combines direct (when interventions are compared head-to-head) and indirect (when interventions are compared through other reference interventions) evidence. We performed NMA when more than three studies formed a connected network. Combining the direct and indirect evidence not only improves precision of estimates, but also provides estimates for all pairwise comparisons, including those missing from the direct evidence. The key assumption of the network meta-analysis is that of consistency of direct and indirect effects. Consistency is likely to hold when the distribution of effect modifiers is (equivalently, patient characteristics are) similar across trials. If this assumption is violated, there may be inconsistency between the direct evidence and indirect evidence of treatment comparisons.[37]

Our NMA used a hierarchical model with a within-study level and a between-studies level that models responses at the arm level and nests arms within studies. We ran two sets of analyses, one assuming consistency of treatment effects and one examining this assumption. The models are shown in Appendix I Briefly, the analysis assuming consistency parameterizes treatment effects as linear combinations of T-1 parameters, where T is the number of treatments in the network. Treatment effects are assumed to be normally distributed across studies with a common variance (i.e., are homoscedastic random effects). We used noninformative default priors on study-level mean treatment effects. Specifically, priors on the means were zero-centered normal distributions, with standard errors 15 times larger than the observed scatter of study effect estimates.

We used empirical prior distributions for the between-study heterogeneity variance. For outcomes modeled on the log odds ratio scale, we assigned a log-normal hyperprior for the between-study heterogeneity variance based on empirical results from meta-epidemiological analyses of nonpharmacologic trials with subjective outcomes.[38, 39] For continuous outcomes (NMD and SNMD) we used inverse gamma priors based on analogous empirical results nonpharmacologic studies of mental health outcomes.[40] We performed a sensitivity analysis using alternative priors for the between-study variance.

In *gemtc*, estimation is done with MCMC via the JAGS[41] sampler, using initial values drawn randomly from the marginal distributions of the priors of respective parameters. We fit four MCMC chains. After a burn in of 5000 iterations, we monitored convergence of random effects means and variances automatically, by checking every 10,000 iterations whether the Gelman Rubin diagnostic was less than 1.05 with 95 percent probability for all monitored parameters. After convergence was reached, an extra 10,000 iterations were run. All models converged within 10000 iterations. Model fit was assessed by comparing the posterior mean of the residual deviance to the number of data points. The ratio of residual deviance to number of data points in the various models was very close to 1 (within 5%), suggesting adequate model fit.

For each analysis, we empirically assessed if the network meta-analysis consistency assumption was violated by comparing the direct and indirect evidence using a node-splitting approach.[42] To this end, for each comparison that is informed by both direct and indirect data, we separately parameterized the direct and indirect effects, and compared the estimates of the two. Although these analyses were not suggestive of inconsistency (not shown), in sparse networks, like the ones in this report, they can be underpowered.

Results are presented in terms of net mean or standardized net mean differences and corresponding 95 percent credible intervals (CrI). We preferentially report net mean differences for substance specific and aggregated (over multiple substances) use days.

Using the sampled posterior distribution of effects, we estimated the probability that a treatment is the most effective, second most effective, and so on, based on the results of the network meta-analyses. We report the surface under the cumulative ranking curve (SUCRA), which represents a single number ranging from 0 to 100 percent associated with each intervention. The higher the SUCRA value (closer to 100%), the higher the likelihood that an intervention is in the top rank or one of the top ranks. As SUCRA values approach 0 percent, it is more likely that an intervention is in the bottom rank, or one of the bottom ranks.[43]

We performed an additional sensitivity analyses by comparing of an additional analysis of standardized net mean differences which combined use days with scales and nonlinear transformations relating to use days. Results were similar with the main analysis (not shown).

Statistical heterogeneity was explored qualitatively. Because of the relatively small number of studies, and the little variability in characteristics, meta-regression and subgroup analyses were not performed.

Grading the Strength of Evidence for Major Comparisons and Outcomes

We graded the strength of the body of evidence (SoE) as per the AHRQ methods guide on assessing the SoE.[44] For conclusions based on NMA of sparse networks, we provided a qualification, and downgraded the SoE due to lack of precision and directness, as applicable.

We assessed the SoE for comparisons of major interventions (i.e., behavioral intervention methods, pharmacologic interventions, and combinations) to no treatment (TAU) and to each other.

To our knowledge, there is no information on the minimal clinically importance differences for the outcomes we consider. The commonly used conventions for standardized mean differences similarly do not translate to minimally importance differences.[45]

For each evaluated comparison, we assessed the number of studies, their study designs, the study limitations (i.e., risk of bias and overall methodological quality), the directness of the evidence to the KQs, the consistency of study results, the likelihood of reporting bias, in addition to the precision and magnitude of the effect estimated across studies using NMA. When at least 3 direct comparisons were available, we compared effects estimated from direct comparisons (using both frequentist and Bayesian random effect models), with effects obtained from Bayesian NMA.

If the Bayesian NMA random effect models (direct and indirect evidence) were consistent with the pairwise (direct), the effect size and precision from the NMA informed SoE ratings. For sparse networks with few direct comparisons, we downgraded the SoE by one category. In these cases consistency is rated as unclear.

Outcomes with highly imprecise estimates, highly inconsistent findings across studies, or with data from only one study were deemed to have insufficient evidence to allow for a conclusion (with the exception that particularly large, generalizable single studies could provide at least low SoE). This approach is consistent with the concept that for imprecise evidence "any estimate of effect is very uncertain," the definition of Very Low quality evidence per GRADE.[46]

Based on these multidimensional assessments, we assigned a SoE rating as being either high, moderate, low, or insufficient.

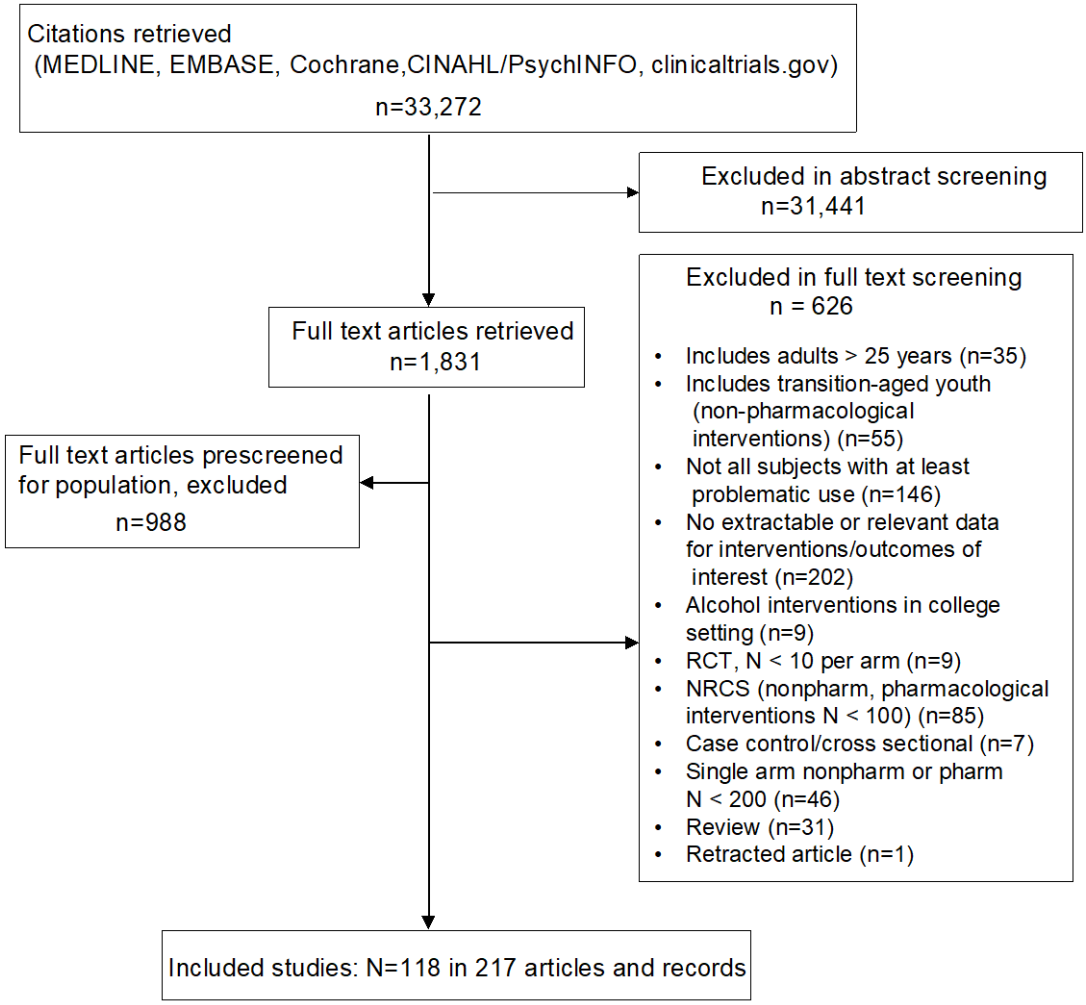
Assessing Applicability

We assessed the applicability within and across studies with reference to adolescents in the populations of interest (i.e., type and severity of abuse and setting).[47]

Results

As illustrated by the flow diagram in Figure 2, we found 118 randomized controlled studies that evaluated treatment of adolescents with problematic substance use or substance use disorders. Excluded studies, along with reasons for exclusion, are listed in Appendix B.

Figure 2. Literature flow diagram



In a separate search for systematic reviews (SR) of interventions for problematic alcohol use in the college setting, we screened 401 abstracts, of these we screened 42 papers in full text, of which 36 were excluded (18 were reviews of preventive interventions, 10 were not in college students, 6 were not SRs, and 2 were not focused on alcohol users). This left 6 SRs that were deemed informative for our narrative summary.

Qualitative Categorization

Among studies of **behavioral interventions**, brief (2 or fewer sessions) and nonbrief (3 or more sessions) were qualitatively distinct. On initial review of the eligible studies, we found that participants in the brief intervention studies had problematic use, whereas nonbrief behavioral intervention studies enrolled adolescents with diagnosed substance disorder(s). In addition, the

interventions provided in nonbrief studies were much more intensive. Therefore, we considered these groups of studies separately in our quantitative synthesis.

Despite superficial heterogeneity of study inclusion criteria with respect to the targeted substance(s), most studies enrolled adolescents using some combination of alcohol and cannabis, with a minority using other drugs.

The 3 studies that specified use of substances other than alcohol and cannabis in their eligibility criteria are briefly described in brief [31, 32] and nonbrief [33] sections, but were excluded from meta-analyses.

The following substance-specific outcomes were evaluated for possible meta-analysis: ***heavy alcohol use days***, ***alcohol use days***, ***alcohol abstinence***, ***cannabis use days*** and ***cannabis abstinence***. In addition, studies reported aggregate outcomes reflecting abstinence for, or use of multiple substances. These outcomes included*:* ***alcohol and other drug use*** (AOD), ***illicit drug use*** and ***other drug use***. In addition, we considered ***substance use problem scales*** within brief and nonbrief categories. Appendix D lists baseline and interventions. Appendix E identifies the outcomes reported by each study and Appendices F and G report detailed results for brief and nonbrief interventions, respectively. Outcomes with sufficient data for an outcome (bulleted below) were meta-analyzed and reported.

Brief Behavioral Interventions

- Alcohol
  - Heavy alcohol use days
  - Alcohol use days
  - Abstinence from alcohol
- Cannabis
  - Cannabis use days
  - Cannabis Abstinence
- Substance use problem scales

  (Legal outcomes)

Nonbrief Behavioral Interventions

- Alcohol
  - Alcohol use days
- Cannabis
  - Cannabis use days
- Aggregate drug use
  - Alcohol and other drug use
  - Illicit drug use days

  (Other outcomes: school performance and education attainment, family-related, peer-related, mental health events, physical health events and legal outcomes)

The results in subsequent sections describe less commonly reported outcomes and are not meta-analyzed. We first briefly review of systematic reviews of **interventions for alcohol use in the college setting**.

Finally, we separately describe **two categories of pharmacologic interventions**.

1. Studies of medications to reduce and/or eliminate and/or to prevent relapse in adolescents with opioid, alcohol, and cannabis use disorders. In studies that combined pharmacologic

and behavioral interventions, the behavioral interventions were often less completely described, and therefore not easily compared to the detailed manual based interventions typical in behavioral trials. Drug trials included placebo arms, which due to the likelihood of a placebo effect, were not deemed comparable to TAU arms in studies of behavioral interventions. Thus, we did not jointly synthesize studies of behavioral interventions with studies of pharmacologic interventions and summarize these studies separately by use disorder.

2. Studies of medications targeting specific co-occurring psychiatric disorders in patients with a substance use disorder(s). Given that effects on substance use may depend on how effectively the underlying psychiatric disorder was treated, we reported scales reflecting the severity of the psychiatric disorder in addition to substance use related outcomes.

Brief Behavioral Interventions

Key Points

Key points from the meta-analyses are summarized below.

- Motivational interviewing (MI)
  - Reduces days of heavy alcohol use compared to TAU (low SoE)
  - Reduces days of overall alcohol use compared to TAU (moderate SoE)
  - Does not reduce days of cannabis use compared to TAU (moderate SoE)
  - Reduces substance use problems compared to TAU (low SoE)

Thirty-six studies (in 64 papers; sample size range, 33 to 1449) [31, 32, 48-109,31, 32, 49-52, 54-69, 71-111] published between 1982 and 2019, evaluated effects of brief behavioral interventions in adolescents (mean age range, 14.8-18.9 years). Thirty-three studies enrolled participants with problematic use of alcohol, cannabis, and/or other drugs and three enrolled adolescents with a diagnosed substance use disorder. Appendix D (Table D-1) provides baseline and intervention details. Each of these studies each had methodological concerns including lack of outcome assessor blinding and incomplete outcome data. Most of the studies evaluated interventions we have coded as MI. Within-study descriptions varied, the intervention most commonly would be classified as Motivational Enhancement Therapy (MET). There was some variation in the number of sessions, the length of individual sessions, and the background and training of the interventionalist. Detailed results are presented by outcome in Appendix F.

Studies Not Included in Meta-Analyses

Enrolled for Use of Substances Other Than Alcohol or Cannabis

Two two-arm studies, published between 2006 and 2011, assessed adolescents with problematic use of specific substances other than alcohol or cannabis and evaluated brief behavioral interventions (Table 2).[31, 32] Adolescents in the studies were on average 15 to 18 years of age (range across studies, 14-22). The studies each had methodological concerns including lack of outcome assessor (or other) blinding, incomplete outcome data, poor compliance with the interventions, and others.

Each study was unique regarding substance used. The primary substances of misuse under study were ecstasy and cocaine [31] (problematic use: at least four times over the past month) and methamphetamine [32] (use disorder per DSM-IV).

Neither study reported significant differences in mean number of use days or abstinence between adolescents who received active behavioral interventions and those who received treatment as usual or non-substance use disorder-related education. In the Marsden 2006 study, those receiving the brief intervention had slightly higher rates of abstinence, but it did not exclude the null effect – for cocaine (RR 1.17, 95% CI 0.94 to 1.46) and for abstinence from crack cocaine (RR 1.12, 95% CI 0.99, 1.26).[31]

In the small study of methamphetamine users, adolescents in both the brief MI and education groups used methamphetamine on average about 1 or 2 days per 30 days with no statistically significant difference between groups. About 50 to 60 percent of adolescents were abstinent at 1 and 2 months, with no statistically significant difference between groups.[32]

Table 2. Results: Brief behavioral interventions for substances other than alcohol or cannabis

Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time Point (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI)
Marsden (2006)	MI	TAU	Ecstasy use (days) (mean, SD)	6	166	8.2 (13.5)	176	8.7 (13.2)	Diff −0.5 (−2.8, 3.0)
			Alcohol use (days) (mean, SD)	6	166	28.9 (25.7)	176	30.7 (25.3)	Diff −1.8 (−7.2, 3.6)
			Cocaine use (days) (mean, SD)	6	166	5.54 (11.5)	176	7.4 (12.6)	Diff −1.9 (−4.4, 0.7)
			Crack use (days) (mean, SD)	6	166	4.67 (15.5)	176	5.7 (15.8)	Diff −1.0 (−4.3, 2.3)
			Cannabis use (days) (mean, SD)	6	166	52.0 (36.5)	176	57.2 (36.3)	Diff −5.2 (−12.9, 2.5)
			Abstinent from ecstasy (%)	6	166	42.8	176	43.8	RR 0.98 (0.77,1.25)
			Abstinent from cocaine (%)	6	166	51.8	176	44.3	RR 1.17 (0.94, 1.46)
			Abstinent from crack cocaine (%)	6	166	81.3	176	72.7	RR 1.12 (0.99, 1.26)
Srisurapa-nont (2007)	MI (Brief, Motivation Building)	Educ	Methamphetamine use (days) (mean, SD)	1	24	1.57 (1.77)	24	0.97 (1.2)	Diff 0.6 (−0.3, 1.5)
			Methamphetamine use (days) (mean, SD)	2	24	1.97 (1.31)	24	1.1 (1.2)	Diff 0.11 (−0.8, 1.0)
			Abstinent from stimulants (%)	1	24	62.5	24	58.3	RR 1.07 (0.68, 1.69)
			Abstinent from stimulants (%)	2	24	54.2	24	62.5	RR 0.87 (0.54, 1.40)

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; Diff = difference; Educ = psychoeducation; MI = motivational interviewing; RR = risk ratio; SD = standard deviation; TAU = treatment as usual

Studies with Nondistinguishable Arms Excluded From Meta-Analysis

Three two-arm studies (in 7 papers) of brief behavioral interventions (Table 3)[84, 87, 88, 101-104] compared interventions that were not distinguishable by our taxonomy, precluding inclusion in the meta-analysis.

Table 3. Brief behavioral intervention studies with two treatment arms with nondistinguishable components

Author, Year	Nondistinguished Intervention Component(s)	No. Arms	Distinguishing Intervention Features
Spirito, 2011 [87, 88]	MI	2	MI with separate family-focused MI session vs. MI with youth only
Smith, 2015 [84]	MI	2	MI with normative feedback vs. MI without normative feedback
Walker, 2016 [101-104]	CBT+MI	2	Motivational check-in vs. Assessment only check in

Abbreviations: CBT = cognitive behavioral therapy; MI = motivational interviewing; No. = number study arms

Studies Eligible for Meta-Analysis

There were 31 studies[48-83, 85, 86, 89-100, 105-109] eligible for meta-analysis, of which 24 were two-arm studies and seven were three-arm studies. One study,[70] reported 12-month outcomes only, and was not included in the meta-analyses.

In six three-arm studies (Table 4), two arms were not distinguishable using our coding schema. The nondistinguished treatment arms were pooled and included in meta-analyses.

Table 4. Brief behavioral intervention studies with three treatment arms with two nondistinguishable components that were pooled in MA

Author, Year	Nondistinguished Component	# Arms	Distinguishing Intervention or Control Features
Winters, 2007 [105]	MI	3	MI with separate family-focused MI session vs. MI with youth only vs. TAU
Winters, 2012 [106-109]	MI	3	MI with separate family-focused MI session vs. MI with youth only vs. TAU
Spijkerman, 2010 [85]	MI	3	MI with normative feedback vs. MI without normative feedback vs. TAU
Dembo, 2014 [66-69]	MI	3	MI with separate family-session vs. MI with youth only vs. TAU
Cunningham, 2015 [58-62]	MI	3	Computer-delivered MI vs. therapist-delivered MI vs. TAU
Peterson, 2006 [83]	TAU	3	Assessment only (TAU) vs. Assessment (TAU) followed by MI

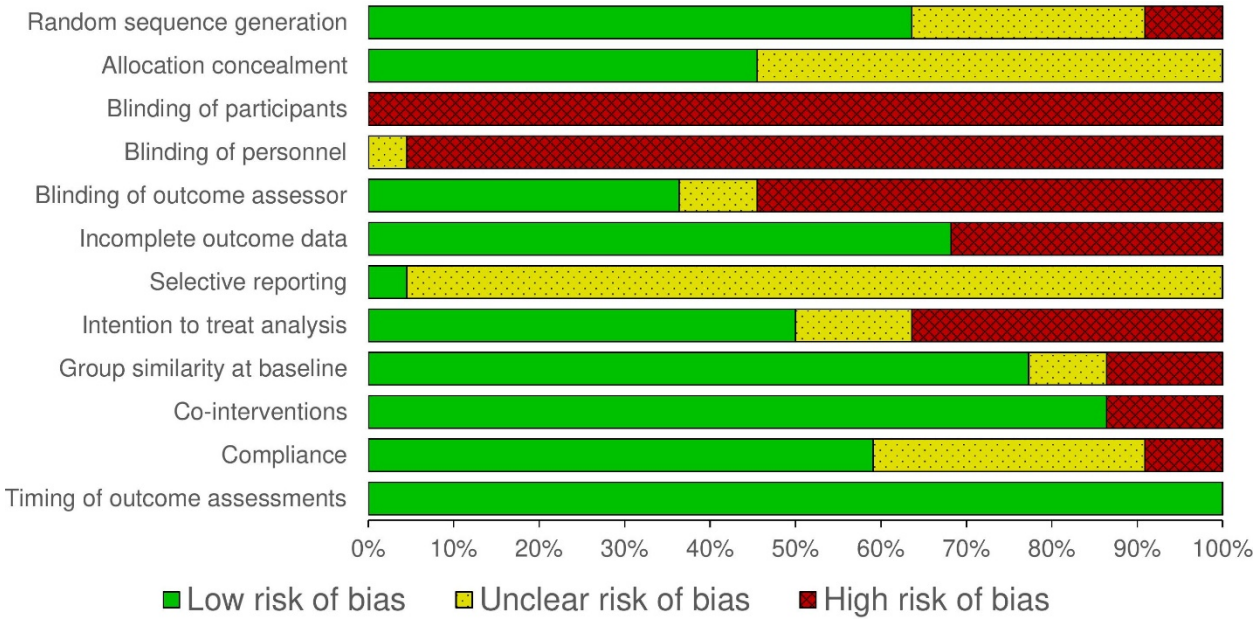
Abbreviations: MA = meta-analysis; MI = motivational interviewing; TAU = treatment as usual; # arms =number of arms

The variations in active interventions (MI or MI+CBT) compared in the nine studies with duplicate arm codes included delivery method (computer vs. therapist),[58-62] post-intervention check-ins (motivational check-in vs. no check-in),[101-104] target recipient (parents/family vs. adolescents only),[87, 88, 105-109],or content (MI with normative feedback vs. without)[84].

Risk of Bias

Risk of bias summaries are presented graphically in Figure 3 for the 30 studies that we considered eligible for meta-analysis. The most common methodological concerns involved lack of blinding of participants, personnel, and outcome assessors.

Figure 3. Meta-analyzed brief behavioral intervention studies: Percentage of studies in each risk of bias category

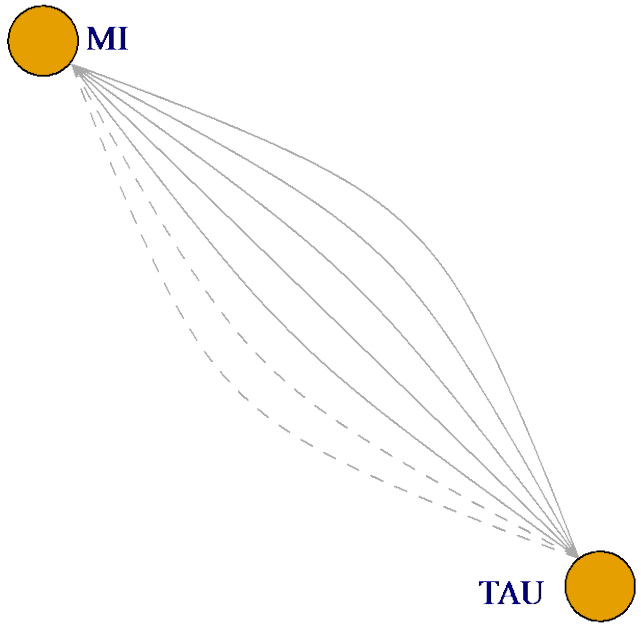


Alcohol Outcomes

Heavy Alcohol Use Days

Seven studies compared MI with TAU[48-50, 52, 55-57, 64, 86, 105] and reported a measure of heavy alcohol use in 2,821 participants. Of these, five studies[50, 52, 55-57, 64, 105] (1,248 subjects), reported heavy use days and two studies[48, 49, 86] (1,573 subjects), reported a scale (Figure 4).[48, 86]

Figure 4. Evidence graph for brief behavioral intervention studies reporting heavy alcohol use days



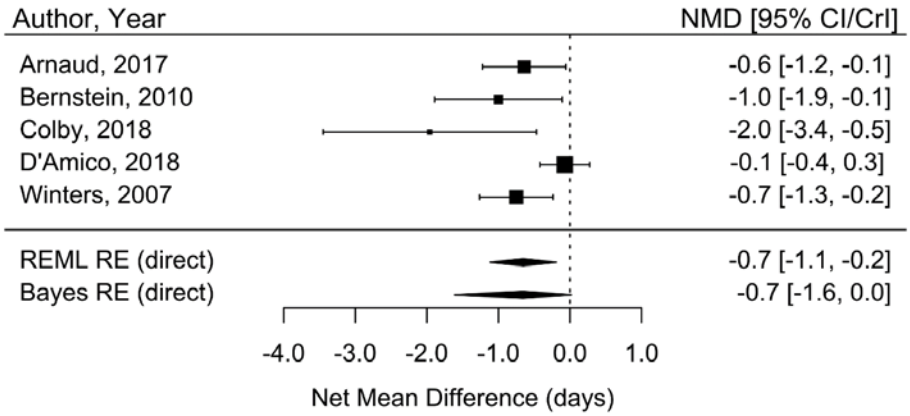
The network plot consists of nodes (yellow circles) representing the interventions being compared and edges (connecting lines) representing the available direct comparisons between interventions. Each edge represents a within study comparison. Dotted edges represent comparisons reported as scales. Abbreviations: TAU = treatment as usual; MI = motivational interview

Key Question 1: Heavy Alcohol Use Days — MI Compared With TAU

As shown in Figure 5, MI relative to TAU has a net mean difference (NMD) of −0.7 (95% CrI −1.6, 0.02) days/month of heavy alcohol use. These results correspond to a Bayesian posterior probability that MI is better than TAU is 97.3 percent.

MI is more effective than TAU in reducing heavy alcohol use days. We rated the strength of evidence (SoE) as low.

Figure 5. Heavy alcohol use: Forest plot depicting individual study effects with summary estimates of the relative effect of MI versus TAU

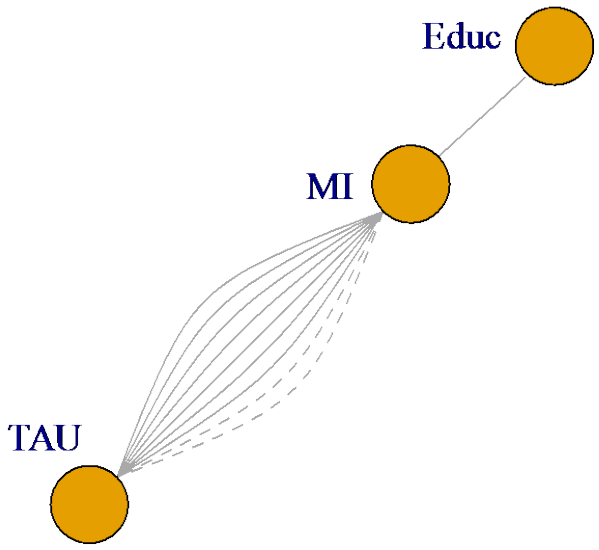


NMD < 1 favors MI. Abbreviations: NMD = net mean difference; REML = restricted maximum likelihood, RE = random effect; CI/CrI = credible interval (for Bayes RE Model); direct = direct (pairwise) comparisons.

Alcohol Use Days

Ten dual-arm studies enrolled a total of 3,726 subjects and reported a measure of the frequency of alcohol use (Figure 6). Of these eight studies[52, 54-57, 64, 78-81, 105-109] (2,153 subjects) reported use days and two studies[48, 49, 86] (1573 subjects) reported a scale. One trial, that enrolled 326 subjects compared MI with Educ and reported use days.[78-80]

Figure 6. Evidence graph for brief behavioral intervention studies reporting alcohol use days



The network plot consists of nodes (yellow circles) representing the interventions being compared and edges (connecting lines) representing the available direct comparisons between interventions. Each edge represents a within study comparison. Dotted edges represent comparisons reported as scales. Abbreviations: TAU = treatment as usual; MI = motivational interview; Educ = education

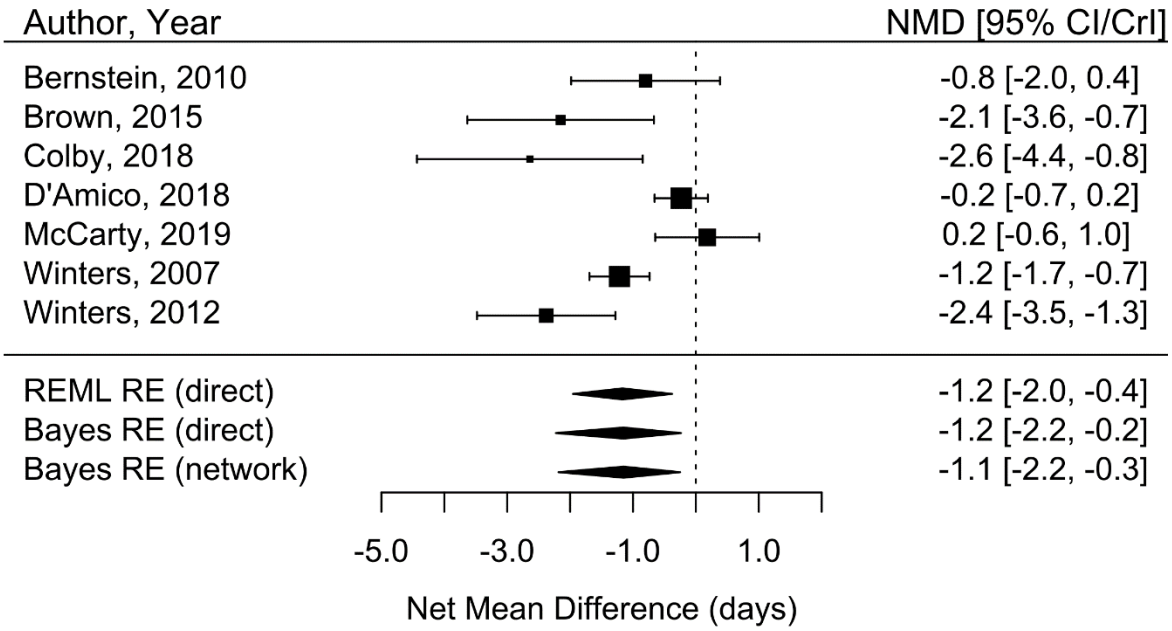
Key Question 1: Alcohol Use Days — MI Compared With TAU

The studies contributing direct evidence for the MI versus TAU comparison are illustrated in Figure 7. The pooled NMD of direct comparisons of MI vs TAU was −1.2 (95% CrI, −2.2, −0.2) days/month of alcohol use, compared to those in TAU groups.

In the NMAs, the pooled NMD for the MI versus TAU comparison was -1.1 (95% CrI −2.2, −0.3) days/month of alcohol use.

MI is more effective than TAU in reducing overall alcohol use days. We rated the overall SoE as **moderate**.

Figure 7. Alcohol use days: forest plot depicting individual study effects with summary estimates of the relative effect of MI versus TAU



NMD < 1 favors MI. Abbreviations: MI = motivational interviewing; TAU = treatment as usual, REML = restricted maximum likelihood, RE = random effect; CI = confidence interval, CrI = credible interval (for Bayes estimates).

Key Question 2: Alcohol Use Days — Comparative Effect of MI Versus Educ

As shown in Table 5, the estimated NMD for MI versus Educ was 0.3 (95% CrI −2.5 to 3.1) days/month (insufficient SoE).

Table 5. Brief behavioral interventions and alcohol abstinence: Net mean difference of days per month of abstinence between all interventions

Intervention	Educ	MI	TAU
Educ	Educ	0.3 (-2.5, 3.1)	1.4 (-1.4, 4.4)
MI	-0.3 (-3.1, 2.5)	MI	**1.1 (0.3, 2.2)**
TAU	-1.4 (-4.4, 1.4)	**-1.1 (-2.2, -0.3)**	TAU

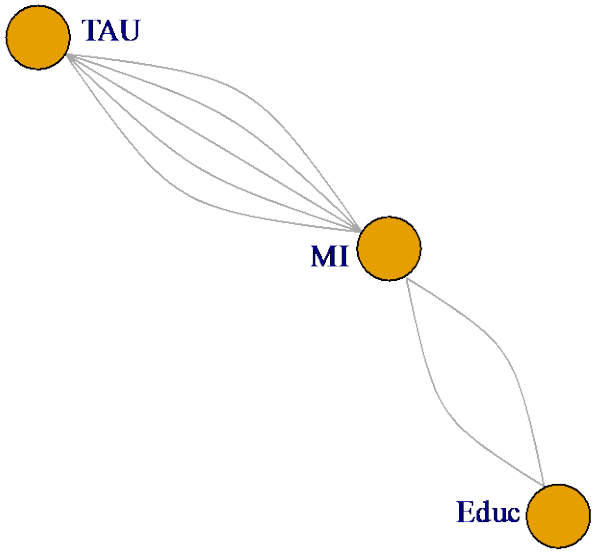
Gray cells display comparisons for which there is indirect evidence only. Effects are expressed as NMD (days/month), with 95% credible intervals in parentheses.

Abbreviations: Educ = psychoeducation; MI = motivational interviewing; TAU = treatment as usual.

Alcohol Abstinence

Abstinence for alcohol was reported by seven studies with outcomes for 2,482 participants (Figure 8).[48, 49, 54, 72, 76-80, 89, 106-109]

Figure 8. Evidence graph for studies reporting alcohol abstinence



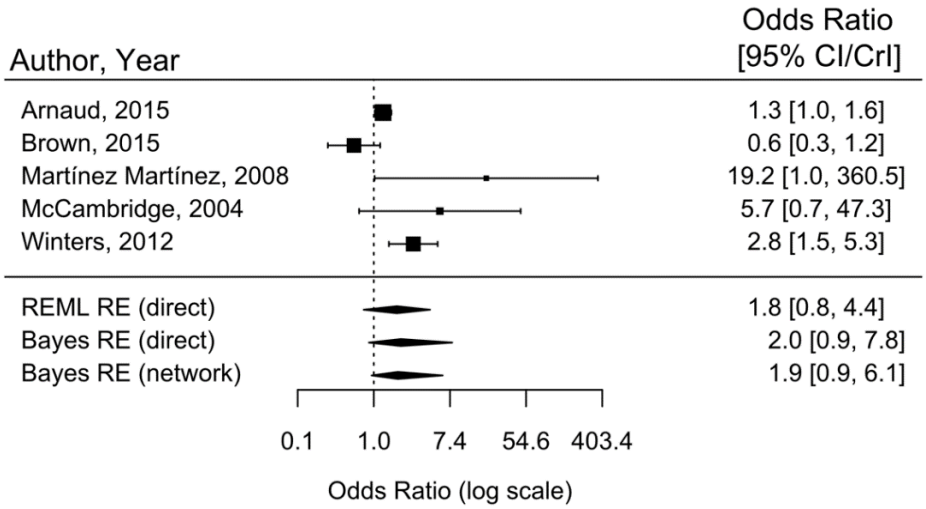
The network plot consists of nodes (yellow circles) representing the interventions being compared and edges (connecting lines) representing the available direct comparisons between interventions. Each edge represents a within study comparison.
Abbreviations: MI = motivational interviewing; TAU = treatment as usual; Educ = education

Key Question 1: Alcohol Abstinence — MI Versus TAU

The studies contributing direct evidence for the MI versus TAU comparison for the odds ratio of attaining abstinence are illustrated in Figure 9. When direct comparisons of MI vs TAU were considered, the odds of abstinence were 2.0 (95% CrI 0.9, 7.8) fold higher for MI than for TAU. In the NMA, the pooled odds ratio 1.9 (95% CrI 0.9, 6.).

MI may be more effective than TAU. However, the credible intervals for both the pairwise NMA are wide, and also compatible with no effect (**insufficient** SoE).

Figure 9. Alcohol abstinence: MI (brief intervention) versus TAU



Odds ratio > 1 favors MI. Abbreviations: MI = motivational interviewing; TAU = treatment as usual, REML = restricted maximum likelihood, RE = random effect; CI = confidence interval; CrI = credible interval (for Bayesian RE Model)

Key Question 2: Comparative Effects of MI and Educ

The comparative effects, as log odds ratios are shown in Table 6.

The estimated effect for Educ versus MI is highly imprecise, with direct evidence from 2 studies only (**insufficient** SoE).

Table 6. Brief behavioral interventions and alcohol abstinence: Odds ratios for abstinence between all interventions

Intervention	Educ	MI	TAU
Educ	Educ	1.3 (0.4, 4.6)	0.7 (0.1, 2.6)
MI	0.8 (0.2, 2.8)	MI	0.5 (0.2, 1.1)
TAU	1.5 (0.4, 9.0)	1.8 (0.9, 5.9)	TAU

Gray cells display comparisons for which there is indirect evidence only. Effects are expressed as odds ratios with 95% credible intervals in parentheses.

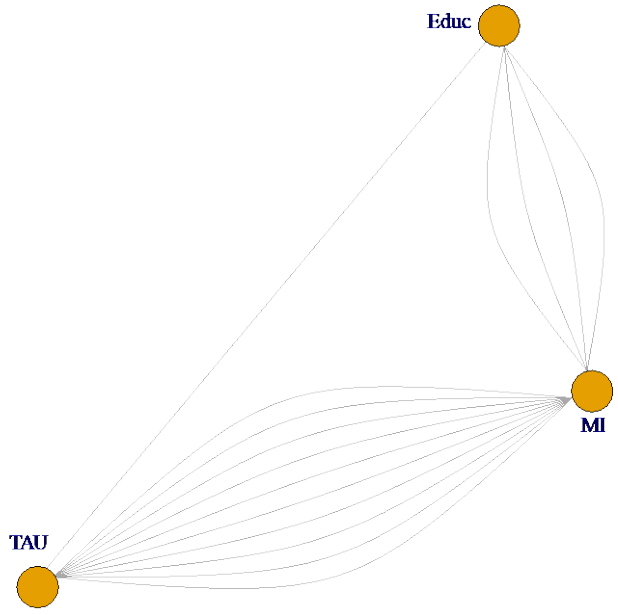
Abbreviations: Educ = psychoeducation; MI = motivational interviewing; TAU = treatment as usual

Cannabis Outcomes

Cannabis Use Days

13 studies analyzed cannabis use days (none reported a scale) in 2,386 participants.[51, 53, 54, 64, 65, 71, 78-81, 83, 89, 99, 100, 106-109] The network geometry is shown in Figure 10.

Figure 10. Evidence graph for brief behavioral intervention studies reporting cannabis use days



The network plot consists of nodes (yellow circles) representing the interventions being compared and edges (connecting lines) representing the available direct comparisons between interventions. Each edge represents a within study comparison.
Abbreviations: MI = motivational interviewing; TAU = treatment as usual; Educ = education

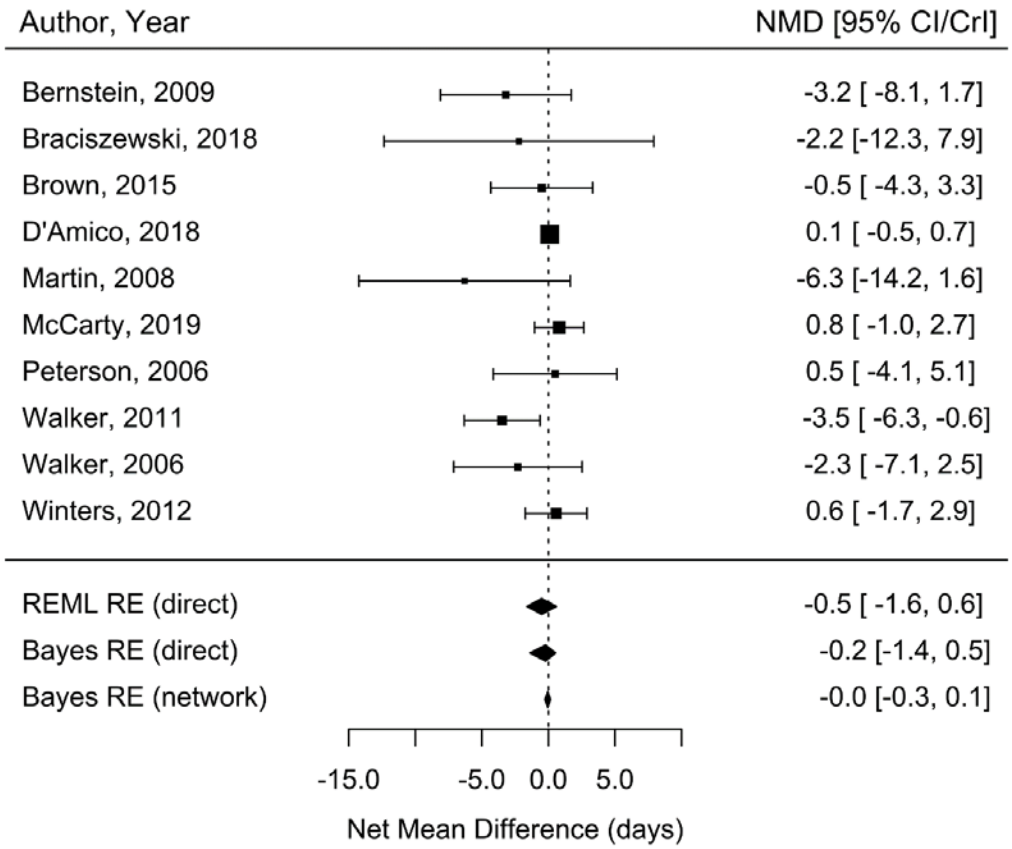
Key Question 1: Cannabis Use Days

MI Compared With TAU

Figure 11 is a forest plot of the 10 studies that performed direct comparisons between MI and TAU. Based on pairwise comparisons only, the direct estimate of NMD was −0.2 (95% CrI -1.4, 0.5) days/month. The effect estimate from the NMA was −0.05 (95% CrI −0.3, 0.1) days/month.

MI is not more effective than TAU. We rated the SoE as **moderate**.

Figure 11. Cannabis use days: Forest plot of net mean difference for MI (brief intervention) versus TAU



NMD < 1 favors MI. Abbreviations: MI = motivational interviewing; CBT= cognitive behavioral therapy; Educ = education; TAU = treatment as usual; CI/CrI = 95% confidence interval/Bayesian credible interval; REML = restricted maximum likelihood estimation; RE = random effect; Bayes = Bayesian analysis; direct = pairwise comparisons only; network = from network meta-analysis

Cannabis Use Days —Educ Compared With TAU

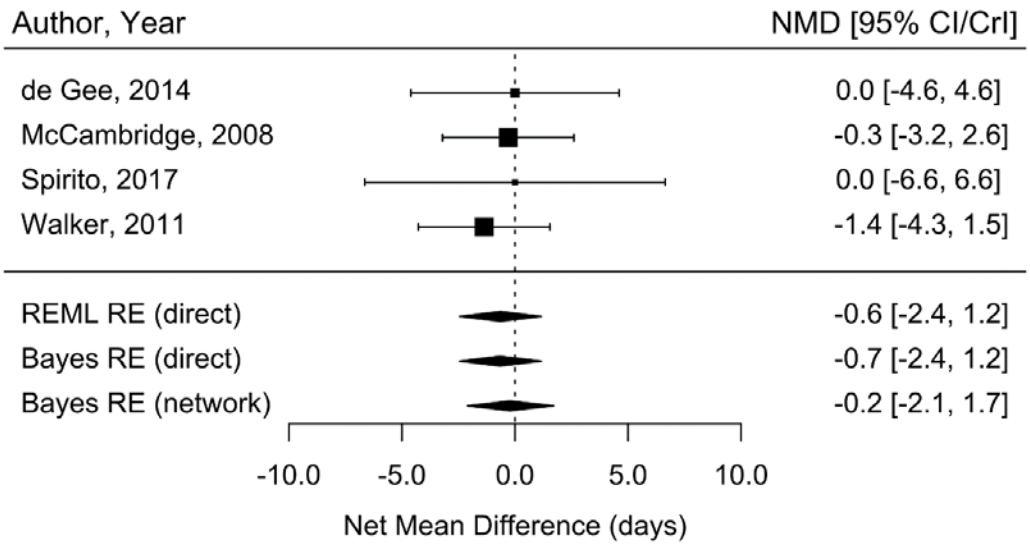
The effect estimates for Educ versus TAU are based on a single direct comparison and have wide credible intervals **(insufficient** SoE).

Key Question 2: Cannabis Use Days — MI Versus Educ

Based on pairwise comparisons only, the direct estimate of NMD was −0.2 (95% CrI -2.4, 1.2) days/month. The effect estimate from the NMA was −0.2 (95% CrI: −2.2, 1.7) days/month.

As shown in Figure 12, the credible intervals are wide for the effect of MI versus Educ (**insufficient** SoE).

Figure 12. Cannabis use days: Forest plot of net mean difference for the brief interventions MI versus Educ

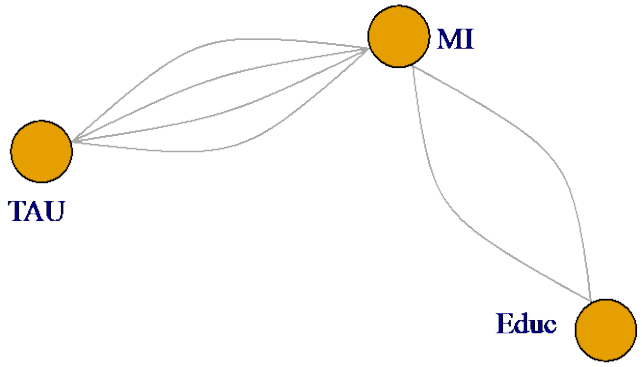


NMD < 1 favors MI. Abbreviations: MI = motivational interviewing; Educ = education; TAU = treatment as usual; CI/CrI = 95% confidence interval/Bayesian credible interval; NMD = net mean difference; REML = restricted maximum likelihood estimation; RE = random effect; Bayes = Bayesian analysis; direct = pairwise comparisons only; network = from network meta-analysis

Cannabis Abstinence

Six studies reported the cannabis abstinence outcomes in 1,119 participants (Figure 13).[51, 54, 76-80, 89, 106-109] Of these, two studies compared MI with a control group who received Educ.[78-80, 89]

Figure 13. Evidence graph for brief behavioral intervention studies reporting cannabis abstinence



The network plot consists of nodes (yellow circles) representing the interventions being compared and edges (connecting lines) representing the available direct comparisons between interventions. Each edge represents a within study comparison. Abbreviations: Educ = education, MI = motivational interviewing, TAU = treatment as usual

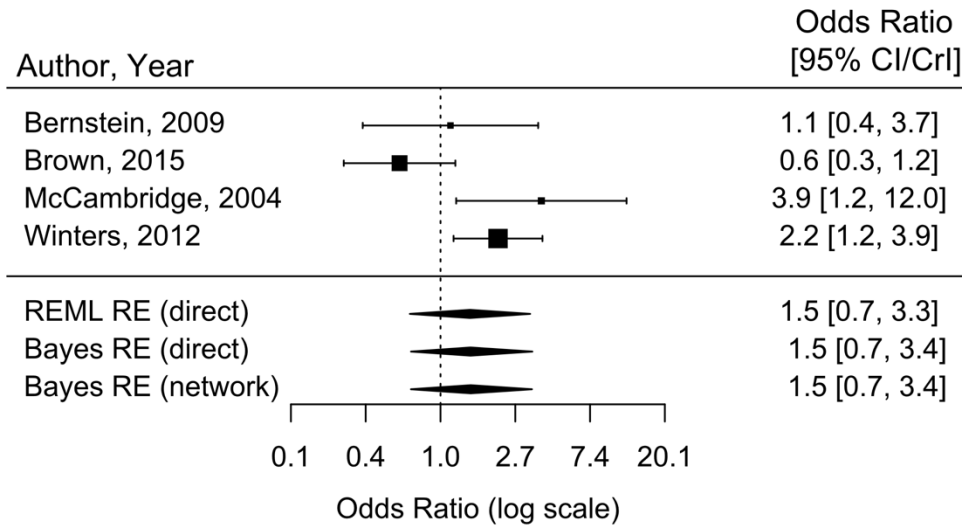
Key Question 1: Cannabis Abstinence

MI Versus TAU

Figure 14 illustrates the study level effects for each of the 4 studies that compared MI and TAU. The summary estimate from the NMA was 1.5 (95% CrI: 0.7 to 3.4).

The credible interval for this estimate is wide and does not exclude no effect or an adverse effect. Therefore, we rated the SoE as **insufficient**.

Figure 14. Cannabis abstinence: Forest plot of log odds ratio for MI (brief intervention) compared with TAU



Odds ratio > 1 favors MI. Abbreviations: MI = motivational interviewing; Educ = education; TAU = treatment as usual; CI/CrI = 95% confidence interval/Bayesian credible interval; REML = restricted maximum likelihood estimation; RE = random effect; Bayes = Bayesian analysis; direct = pairwise comparisons only; network = from network meta-analysis

Key Question 2: Cannabis Abstinence — Comparative Effects of MI Versus Educ

The credible interval for the indirect estimate of the Educ vs TAU effect was similarly imprecise.

As shown in Table 7, the odds ratio for abstinence between MI versus Educ is 2.0 (95% CrI 0.7, 7.4). We rated the SoE as **insufficient** due to imprecision.

Table 7. Brief behavioral interventions and cannabis abstinence: Odds ratios for abstinence between all interventions

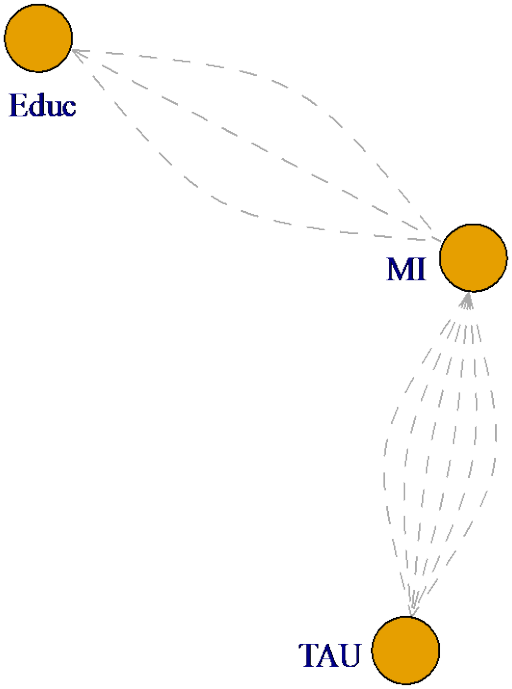
Intervention	Educ	MI	TAU
Educ	Educ	2 (0.7, 7.5)	1.4 (0.4, 6.3)
MI	0.5 (0.1, 1.4)	MI	0.7 (0.3, 1.5)
TAU	0.7 (0.2, 2.8)	1.5 (0.7, 3.4)	TAU

Gray cells display comparisons for which there is indirect evidence only. Effects are expressed as odds ratios with 95% credible intervals in parentheses. Abbreviations: Educ = psychoeducation; MI = motivational interviewing; TAU = treatment as usual

Substance Use Problem Scale

Nine studies, with the comparisons show in Figure 15, reported one of 8 substance use problem scales in 1,854 participants.[50, 55-57, 64, 65, 71, 78-80, 100, 105-109]

Figure 15. Evidence graph of brief behavioral intervention studies reporting a substance use problem scale



The network plot consists of nodes (yellow circles) representing the interventions being compared and edges (connecting lines) representing the available direct comparisons between interventions. Each edge represents a within study comparison. Abbreviations: Educ = education, MI = motivational interviewing, TAU = treatment as usual

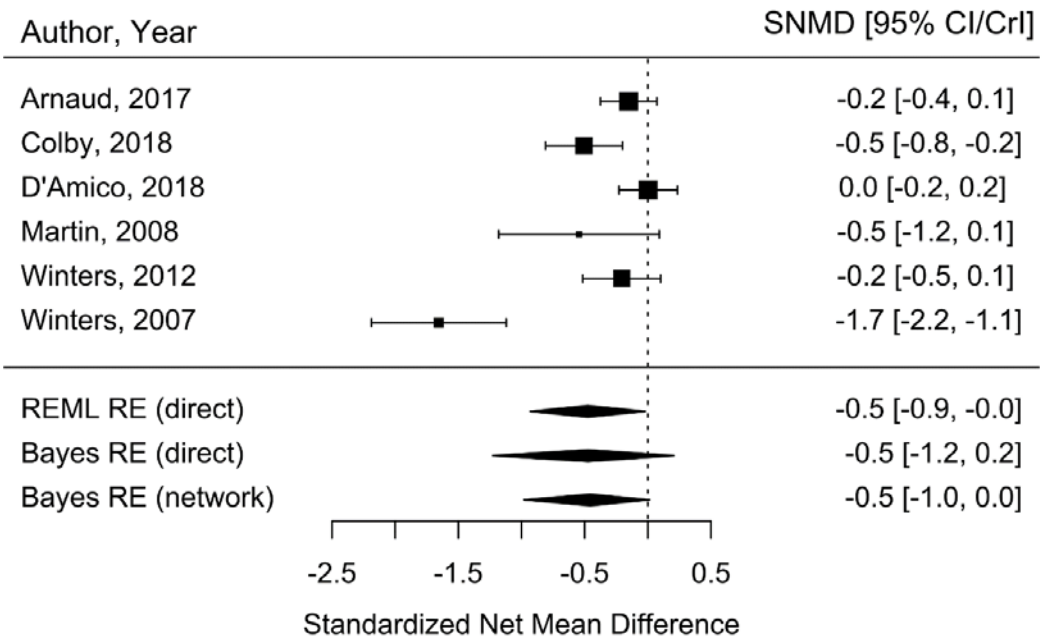
Key Question 1: Substance Use Problem Scales

MI Compared With TAU

Figure 16 illustrates the study level effects for each of the 6 studies that compared MI and TAU. Based on pairwise comparisons only, the SNMD was -0.5 (95% CrI -1.25, 0.2). The pooled estimate from the NMA was –0.5 (95% CrI –1.0 to 0), similar to the direct estimates that included the 3 studies that compared MI with Educ was -0.4 (95% CrI -1.0, 0.01).

MI is better than TAU in reducing substance abuse related problems. We rated the SoE as **low**.

Figure 16. Substance use problem scales: Forest plot of standardized net mean difference of the brief interventions MI versus TAU



SNMD < 1 favors MI. Abbreviations: Educ = education, MI = motivational interviewing, TAU = treatment as usual; SMD = standardized mean difference; CrI = credible interval

Educ Compared With TAU

No studies directly compared Educ with TAU. The SNMD for this effect was -0.5 (95% CrI −1.4, 0.32).

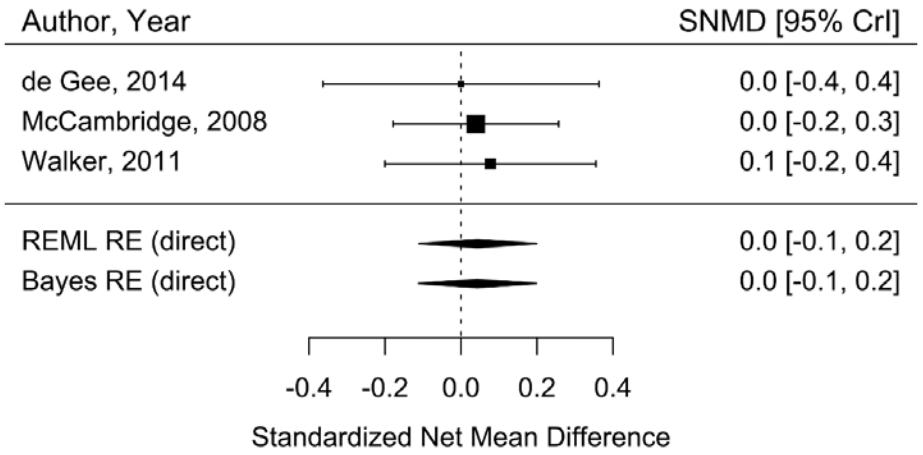
We rated the SoE as **insufficien**t, due to imprecision.

Key Question 2: Substance Use Problem Scales — MI Versus Educ

Figure 17 illustrates the study level effects for each of the 3 studies that directly compared MI with Educ. The pairwise random effect estimate of the SNMD was 0.04 (95% CrI −0.1, 0.2). The SNMD of 0.04 obtained from the NMA that included all studies was identical to the pairwise estimate. However, this estimate (not shown in Figure 17 had a much wider credible interval, from -0.6 to 0.7.

We rated the SoE as **insufficien**t, due to imprecision.

Figure 17. Substance use problem scales: Forest plot of standardized net mean difference of the brief interventions MI versus Educ



SNMD < 1 favors MI. Abbreviations: SNMD = standardized net mean difference; CrI = credible interval; REML = restricted maximum likelihood; RE = random effect; direct = estimated from pairwise comparisons only.

Legal Outcomes

One study (McCambridge 2003) compared Motivational Interviewing (MI) and Treatment As Usual (TAU) and provided data on adolescents' self-reported selling of drugs to their friends and to non-friends. As detailed in Table 8, more adolescents in the MI group than the TAU group sold drugs to their friends (40% vs. 15%; OR=3.7, 95% CI 1.8 to 7.5).

Table 8. Legal outcomes with brief behavioral interventions

Author, Year PMID	Intervention Label	Control Label	Time (Months)	Sold Drugs to Friends	Sold Drugs to Friends	Sold Drugs to Friends	Sold Drugs to Non-friends	Sold Drugs to Non-friends	Sold Drugs to Non-friends
				Int.	Cont.	Calc. Effect (95% CI)	Int.	Cont.	Calc. Effect (95% CI)
McCambridge 2003[76, 77]	Motivational Interviewing (N=82)	Treatment as usual (N=97)	3	40%	15%	***OR 3.7 (1.8, 7.5)***	14%	7%	OR 2.2 (0.8, 5.9)

Abbreviations: Calc. = calculated; CI = confidence interval; Cont. = control; Int. = intervention; OR = odds ratio

Nonbrief Behavioral Interventions

Key Points

Key points from the meta-analyses of nonbrief behavioral interventions are summarized by outcome below.

Nonbrief Behavioral Interventions by Outcome

- **Days of alcohol use**
  - Limited, primarily indirect evidence, suggests that family focused therapy (Fam) may reduce days of alcohol use relative to TAU (**low** SoE)
  - Limited, primarily indirect evidence suggests that family focused therapy (Fam) may be more effective than ICM, CBT and MI in reducing days of alcohol use (**low** SoE).
- **Days of cannabis use**
  - Limited, primarily indirect evidence, suggests that CBT, CBT+MI and CBT+MI+CM, Educ) may result in relative **increases** relative to TAU in days of cannabis use (**low** SoE)
- **Days of alcohol and other drug use (AOD)**
  - Limited, primarily indirect evidence suggests that both MI and CBT may reduce days of AOD use relative to TAU (**low** SoE)
  - MI was more effective than PeerGroup, CBT+MI, Fam, CBT+ICM, CBT+MI+ICM, CBT and ICM (**low** SoE)
- **Days of illicit drug use**
  - Limited, primarily indirect evidence, suggests that CBT+MI reduces days of illicit drug use relative to TAU (**low** SoE)

There were 59 studies in 103 studies (sample size, range 26 to 514), which enrolled 8,786 participants with substance use disorders involving alcohol, cannabis and other drugs.[18, 33, 112-210] Table 10 provides baseline and arm details.

Of these, there were 44 two-arm studies, 12 three-arm studies and 3 four-arm studies. Across studies, there were a total of 136 arms, of which 97 were coded as a single intervention, including TAU (29 arms), Fam (25 arms), CBT (19 arms), MI (5 arms), PeerGroup (10 arms), Educ (6 arms), ICM (2 arm), and CM (1 arm). The remaining 39 arms were coded as compound interventions (two or more separate components). Details of baselines and interventions are given in Appendix D (Table D-2). Detailed results are presented by outcome in Appendix G.

Studies Including Arms With Nondistinguished Intervention Codes

Thirteen nonbrief behavioral intervention studies (5 two-arm studies [Table 9]; 8 multi-arm studies [Table 10]) evaluated different variants of CBT, MI, Fam, Peer group, and TAU components (or their combinations) not captured by our taxonomy, and therefore have two arms with the same coding (i.e., they are nondistinguishable in our categorizations).

Table 9. Nonbrief behavioral intervention studies with two treatment arms with nondistinguishable components

Author, Year	Nondistinguished Intervention Component(s)	No. Studies	Distinguishing Comparison of Interest
Amini, 1982 [18]	TAU	2	Outpatient vs. inpatient care. Both interventions were too poorly specified to warrant coding of components.
Schaeffer, 2013 [187]			Building apprenticeship program vs. standard vocational education
Burrow-Sanchez, 2012 [115]	CBT	2	CBT culturally adapted for Latino youth population vs. standard CBT
Burrow-Sanchez, 2015 [116, 117]			CBT culturally adapted for Latino youth population vs. standard CBT
Rohde, 2014 [182, 183]	CBT+Fam	1	Sequencing and combined effects of CBT and Fam. Evaluated CBT followed by Fam, Fam followed by CBT, and CBT combined with Fam concurrently

Abbreviations: CBT = cognitive behavioral therapy; Fam = family therapy; TAU = treatment as usual

Table 10. Nonbrief behavioral intervention studies with multiple treatment arms with nondistinguishable components

Study Author, Year, PMID	Components Studied	No. Studies	Distinguishing Component of Interest
Kaminer, 2008 [146-148]	CBT+MI vs. CBT+MI vs. TAU	1	In-person MI vs. telephone MI vs. TAU
Dennis, 2004 [120]	CBT+MI vs. CBT+MI vs. CBT+MI+Educ+ICM	1	CBT+MI for 5 sessions vs. CBT+MI for 12 sessions vs. CBT+MI for 12 sessions with parent group education and case management
Stanger, 2015 [200]	CBT+MI vs. CBT+MI+CM vs. CBT+MI+CM	1	CBT+MI vs. CBT+MI+CM vs. CBT+MI+CM with additional parent sessions
Robbins, 2008 [173]	Fam vs. Fam vs. TAU	2	Family therapy using a systems/structural model vs. family therapy using an ecological model vs. TAU
Slesnick, 2009 [190]			Family therapy using a functional model vs. family therapy using an ecological model vs. TAU
Joanning, 1992 [138]	Fam vs. Fam vs. PeerGroup	2	Family therapy using an educational model vs. family therapy using a structural model vs. youth-only group therapy
Liddle, 2001 [153]			Family therapy using an educational model vs. family therapy using an ecological model vs. youth-only group therapy
Henggeler, 2006 [135]	Peer group vs. PeerGroup vs. Fam+PeerGroup vs. Fam+CM+PeeerGroup	1	Family court with usual community services (including peer group therapy) vs. drug with usual community services (including peer group therapy) vs. drug court combined with family therapy using an ecological model and peer group therapy vs. drug court combined with family therapy using an ecological model and peer group therapy and contingency management

Abbreviations: CBT = cognitive behavioral therapy; CM = contingency management; Educ = psychoeducation; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; TAU = treatment as usual

Substances Other Than Alcohol or Cannabis

One 2-arm study [33] summarized in Table 11, enrolled adolescents with inhalant use and evaluated a 4-session CBT-based intervention with an educational component. The authors concluded that adolescents who received CBT and education were about 3 times more likely to be abstinent at 1 year than those who received education alone (16% vs. 5%; RR 3.20, 95% CI 1.34 to 7.65).[33]

Table 11. Results: Nonbrief behavioral interventions for substances other than alcohol or cannabis

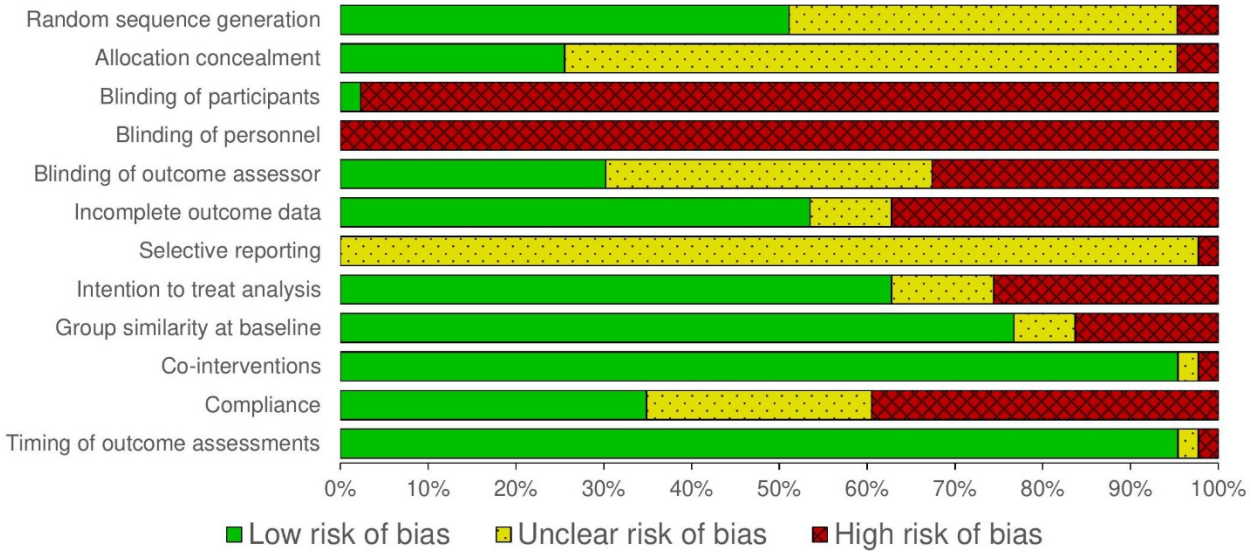
Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time Point (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI)
Ogel (2011) [33]	CBT_Educ (Nonbrief, Cognitive Behavioral/Educational)	Educ	Abstinent from inhalants (N)	12	31	16	31	5	RR 3.20 (1.34, 7.65)

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; Diff = difference; MI = motivational interviewing; RR = risk ratio; SD = standard deviation; TAU = treatment as usual

Risk of Bias

Risk of Bias summaries are given in Figure 18 for the 53 studies that were eligible for meta-analysis. Each of these studies had methodological concerns, most prominently lack of blinding of participants and personnel and compliance.

Figure 18. Meta-analyzed nonbrief behavioral intervention studies: Percentage of studies in each risk of bias category



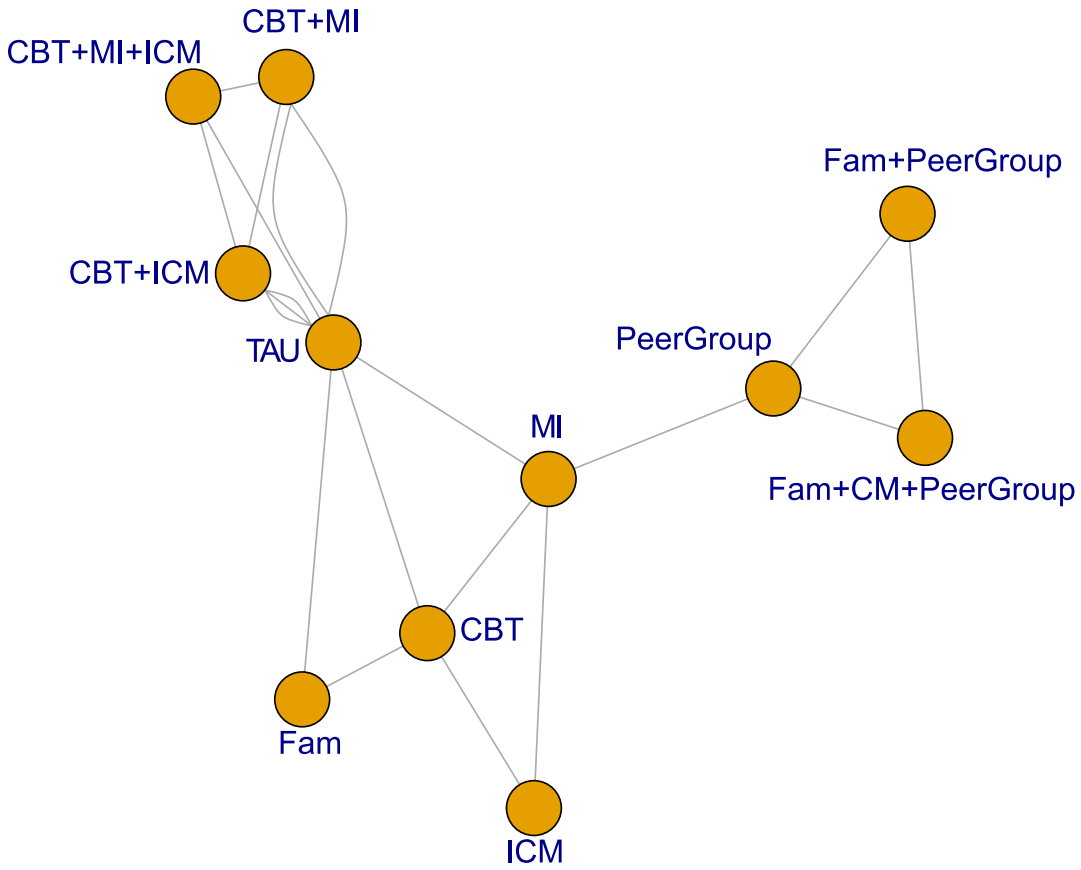
Network Meta-Analyses

Alcohol Outcomes

Alcohol Use Days

Eleven studies, comprised of eight dual-arm and three multi-arm studies as illustrated in Figure 19, enrolled 2,248 subjects and reported a measure of mean alcohol use days. Of these, two studies[129, 205] reported a scale.

Figure 19. Evidence graph for nonbrief behavioral intervention studies reporting mean alcohol use days



Abbreviations: MI = motivational interviewing; Fam = family focused therapy; CBT = cognitive behavioral therapy; CM = contingency management; PeerGroup = peer group therapy; ICM = intensive case management; TAU = treatment as usual

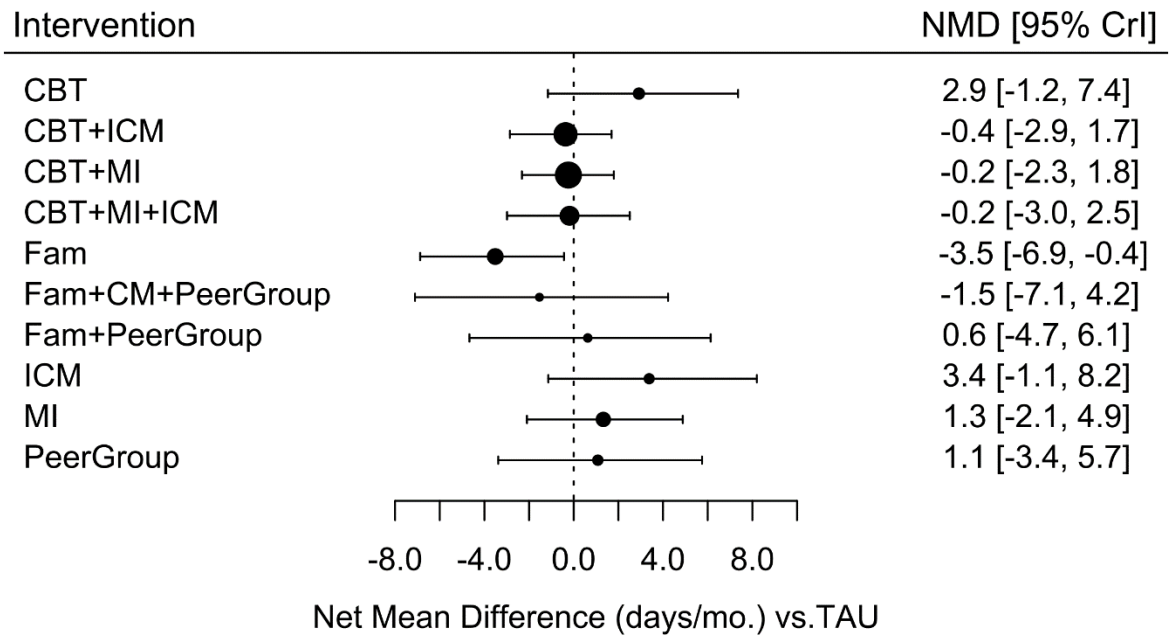
Key Question 1: Alcohol Use Days — Behavioral Interventions Compared With TAU

Figure 20 illustrates that net mean differences (NMD) from the network meta-analysis (NMA) for the 10 interventions evaluated. Note, however, that the network is sparse, and the comparisons between different treatments are often based on a series of single-study indirect comparisons. Because the network is not densely connected (most indirect comparisons rely on a small set of RCTs) and because most RCTs are small, the statistical power to detect inconsistency between direct and indirect effects is very limited. Thus, estimates of treatment effectiveness are very imprecise.

Fam was more effective than TAU. Participants who received Fam versus TAU had an NMD of −3.5 (95% CrI −6.9, -0.4) days of alcohol use per month. We rated the associated SoE for this effect as **low**.

There is **insufficient** evidence regarding the relative effects of the other interventions compared with TAU.

Figure 20. Alcohol use days: Summary forest plot of meta-analyzed net mean difference for all interventions studied compared with TAU



NMD < 1 favors intervention relative to TAU. Abbreviations: NMD = net mean difference; MI = motivational interviewing; Fam = family focused therapy; CBT = cognitive behavioral therapy; CM = contingency management; PeerGroup = peer group therapy; ICM = intensive case management; TAU = treatment as usual; CrI = Bayesian credible interval.

Key Question 2: Comparative Effects of Behavioral Interventions

Most of the results in this network are based on indirect data, with direct data limited to only one or two studies. The statistical power to detect inconsistency between direct and indirect effects is very limited. Thus, estimates of treatment effectiveness are very imprecise.

The comparative effects of all interventions are detailed in Table 12. Among single component interventions, suggesting that Fam is better than ICM, CBT and MI. We rated the associated SoE as **low**.

Table 12. Nonbrief behavioral interventions and alcohol use days: Net mean difference of use days per month between all interventions

Intervention(s)	CBT	CBT+ICM	CBT+MI	CBT+MI+ ICM	Fam	Fam+CM+ PeerGroup	Fam+ PeerGroup	ICM	MI	PeerGroup	TAU
CBT	**CBT**	-3.3 (-8.5, 1.2)	-3.1 (-8.1, 1.4)	-3.1 (-8.4, 1.7)	***-6.5 (-11.2, -2.2)***	-4.4 (-10.1, 0.9)	-2.3 (-7.7, 2.9)	0.5 (-3, 3.8)	-1.6 (-4.9, 1.5)	-1.8 (-6.4, 2.4)	-2.9 (-7.4, 1.2)
CBT+ICM	3.3 (-1.2, 8.5)	**CBT+ICM**	0.1 (-2.2, 2.9)	0.2 (-2.5, 3.2)	-3.1 (-7, 0.8)	-1.2 (-7, 5.2)	1 (-4.5, 7.2)	3.8 (-1.1, 9.2)	1.7 (-2.2, 6.1)	1.5 (-3.4, 6.9)	0.4 (-1.7, 2.9)
CBT+MI	3.1 (-1.4, 8.1)	-0.1 (-2.9, 2.2)	**CBT+MI**	0 (-2.8, 2.8)	-3.3 (-7.2, 0.4)	-1.3 (-7.2, 4.8)	0.9 (-4.8, 6.8)	3.6 (-1.3, 8.9)	1.6 (-2.4, 5.7)	1.3 (-3.5, 6.5)	0.2 (-1.8, 2.3)
CBT+MI+ICM	3.1 (-1.7, 8.4)	-0.2 (-3.2, 2.5)	0 (-2.8, 2.8)	**CBT+MI+ ICM**	-3.3 (-7.6, 0.7)	-1.4 (-7.5, 5.1)	0.8 (-5.1, 7)	3.6 (-1.7, 9.2)	1.5 (-2.8, 6)	1.2 (-3.9, 6.8)	0.2 (-2.5, 3)
Fam	***6.5 (2.2, 11.2)***	3.1 (-0.8, 7)	3.3 (-0.4, 7.2)	3.3 (-0.7, 7.6)	**Fam**	2 (-4, 8.3)	4.1 (-1.5, 10.3)	***6.9 (2.1, 12.1)***	***4.8 (0.8, 9.2)***	4.6 (-0.3, 10)	***3.5 (0.4, 6.9)***
Fam+CM+ PeerGroup	4.4 (-0.9, 10.1)	1.2 (-5.2, 7)	1.3 (-4.8, 7.2)	1.4 (-5.1, 7.5)	-2 (-8.3, 4)	**Fam+CM+ PeerGroup**	2.2 (-1.2, 5.5)	4.9 (-0.6, 10.6)	2.8 (-1.6, 7.3)	2.6 (-0.8, 6)	1.5 (-4.2, 7.1)
Fam+ PeerGroup	2.3 (-2.9, 7.7)	-1 (-7.2, 4.5)	-0.9 (-6.8, 4.8)	-0.8 (-7, 5.1)	-4.1 (-10.3, 1.5)	-2.2 (-5.5, 1.2)	**Fam+ PeerGroup**	2.7 (-2.6, 8.2)	0.7 (-3.5, 4.9)	0.4 (-2.5, 3.4)	-0.6 (-6.1, 4.7)
ICM	-0.5 (-3.8, 3)	-3.8 (-9.2, 1.1)	-3.6 (-8.9, 1.3)	-3.6 (-9.2, 1.7)	**-6.9 (-12.1, -2.1)**	-4.9 (-10.6, 0.6)	-2.7 (-8.2, 2.6)	**ICM**	-2.1 (-5.6, 1.3)	-2.3 (-6.9, 2.1)	-3.4 (-8.2, 1.1)
MI	1.6 (-1.5, 4.9)	-1.7 (-6.1, 2.2)	-1.6 (-5.7, 2.4)	-1.5 (-6, 2.8)	**-4.8 (-9.2, -0.8)**	-2.8 (-7.3, 1.6)	-0.7 (-4.9, 3.5)	2.1 (-1.3, 5.6)	**MI**	-0.2 (-3.2, 2.8)	-1.3 (-4.9, 2.1)
PeerGroup	1.8 (-2.4, 6.4)	-1.5 (-6.9, 3.4)	-1.3 (-6.5, 3.5)	-1.2 (-6.8, 3.9)	-4.6 (-10, 0.3)	-2.6 (-6, 0.8)	-0.4 (-3.4, 2.5)	2.3 (-2.1, 6.9)	0.2 (-2.8, 3.2)	**PeerGroup**	-1.1 (-5.7, 3.4)
TAU	2.9 (-1.2, 7.4)	-0.4 (-2.9, 1.7)	-0.2 (-2.3, 1.8)	-0.2 (-3, 2.5)	***-3.5 (-6.9, -0.4)***	-1.5 (-7.1, 4.2)	0.6 (-4.7, 6.1)	3.4 (-1.1, 8.2)	1.3 (-2.1, 4.9)	1.1 (-3.4, 5.7)	**TAU**

Bold font indicates 95% CrI excludes the null effect.

Abbreviations: CBT = cognitive behavioral therapy; CM = contingency management; Educ = psychoeducation; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; TAU = treatment as usual.

In Table 13, the interventions are ranked by the surface area under the cumulative ranking curve (SUCRA). The higher the SUCRA value (closer to 100%), the higher the likelihood that an intervention is in the top rank or one of the top ranks. As SUCRA values approach 0 percent, the more likely that an intervention is in the bottom rank, or one of the bottom ranks.[43] The last three columns summarize the probability that each intervention ranks in the top third, middle third, and bottom third, respectively. There is a 95 percent chance that Fam ranks in the top third, a 91 percent chance that ICM ranks in the bottom third, and an 88 percent chance that CBT is in the bottom third with respect effects on overall alcohol use days.

Table 13. Probabilities of nonbrief behavioral interventions ranking in top third, middle third and bottom third to reduce alcohol use days

Intervention(s)	SUCRA	Top third	Middle third	Bottom third
Fam	96%	95	5	0
Fam+CM+PeerGroup	79%	66	28	6
CBT+ICM	66%	36	51	14
CBT+MI	64%	28	58	15
CBT+MI+ICM	62%	29	52	19
TAU	58%	12	71	17
Fam+PeerGroup	51%	22	43	35
PeerGroup	44%	7	38	55
MI	40%	3	37	60
CBT	22%	1	11	88
ICM	18%	1	8	91

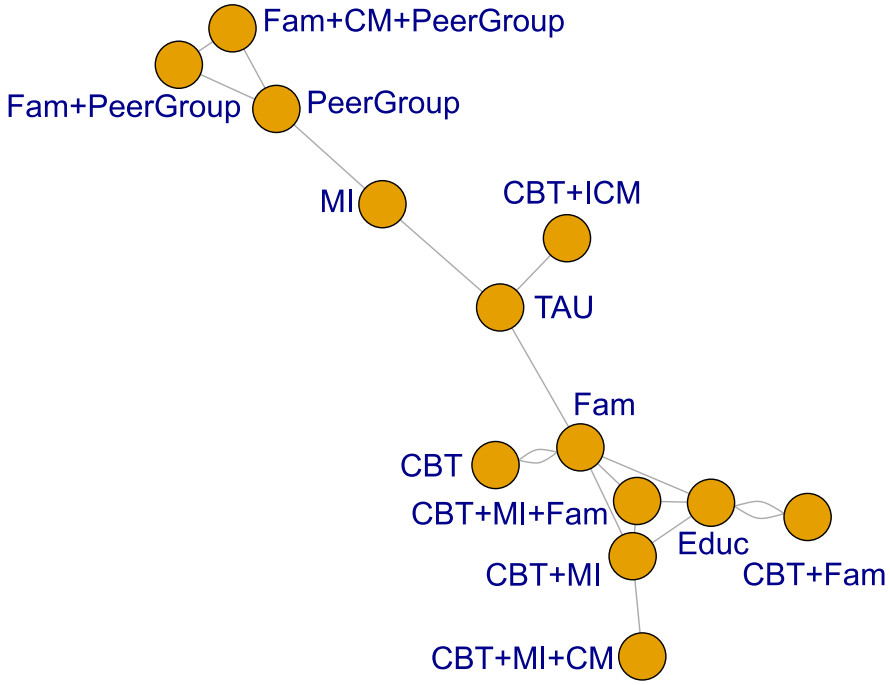
Abbreviations: CBT = cognitive behavioral therapy; CM = contingency management; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; PeerGroup = peer group therapy; SUCRA = surface area under the cumulative ranking curve; TAU = treatment as usual

Cannabis Outcomes

Cannabis Use Days

Eleven studies reported cannabis use days (none reported a scale reflecting use days).[114, 118, 124-126, 135, 151, 154-161, 165-172, 200, 204, 208, 209] The network of treatment comparisons shown in Figure 21 for the nine dual-arm and two multi-arm, with 1,643 participants included in this network meta-analysis.

Figure 21. Evidence graph for studies reporting cannabis use days



Abbreviations: Fam = family; CM = contingency management; TAU = treatment as usual; CBT = cognitive behavioral therapy; ICM = intensive case management; MI = motivational interviewing; Educ = education.

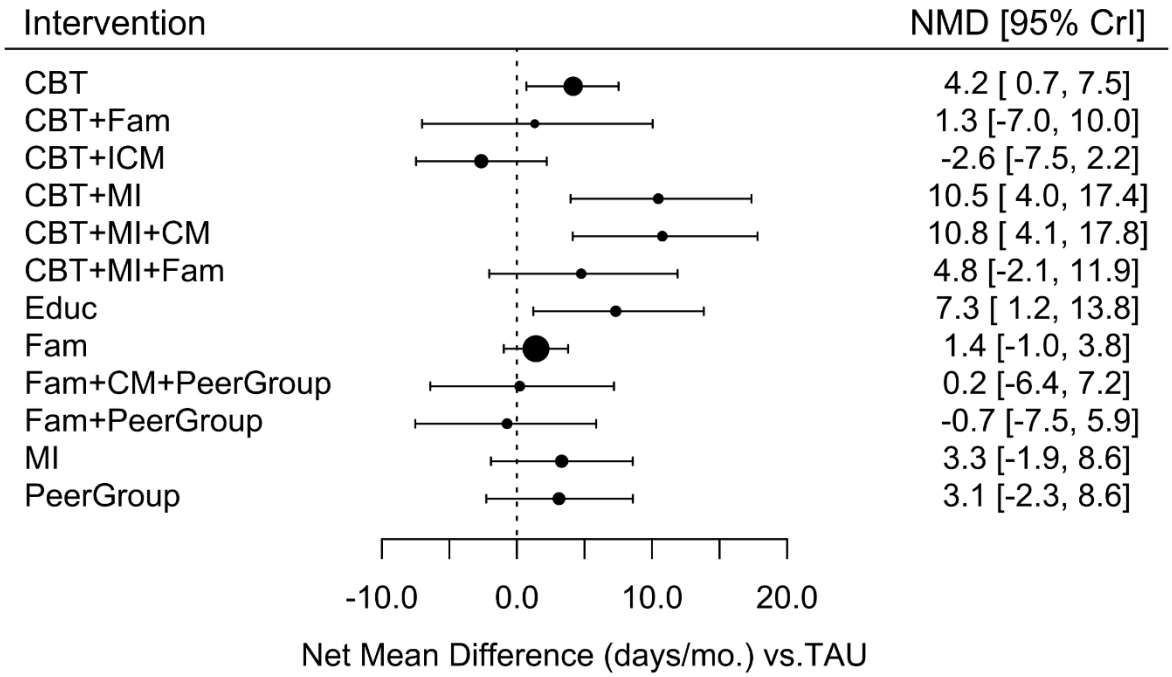
Key Question 1: Cannabis Use Days — Behavioral Interventions Compared With TAU

Compared to TAU, we cannot conclude that any of interventions studied reduced cannabis use days (Figure 22). All point estimates of treatment effects, except for CBT+ICM and Fam+PeerGroup, were positive, consistent with an increase in cannabis use days.

However, the credible intervals were generally wide. As was the case in the previous analysis, the network is very sparse and loosely connected, and because most RCTs are small, the statistical power to detect inconsistency between direct and indirect effects is very limited. Thus, estimates of treatment effectiveness are very imprecise.

One intervention (CBT), and two combined interventions (CBT+MI and CBT+MI+CM) **increased** cannabis use days relative to TAU. We rated the associated SoE for this conclusion as **low**.

Figure 22. Cannabis use days: Summary forest plot of meta-analyzed net mean differences for all interventions compared with TAU



NMD <1 favors intervention versus TAU. Abbreviations: MI = motivational interviewing; Fam = family focused therapy; CBT = cognitive behavioral therapy; CM = contingency management; PeerGroup = peer group therapy; ICM = intensive case management; TAU = treatment as usual; CrI = credible interval

Key Question 2: Cannabis Use Days — Comparative Effects of Behavioral Interventions

Table 14 enumerates the relative effects of all interventions and interventions combinations studied. Most of the results in the table are based on indirect data, with direct data limited to one or two studies. The statistical power to detect inconsistency between direct and indirect effects is very limited. Thus, estimates of treatment effectiveness are imprecise.

Given that we cannot conclude that any of interventions studied reduced cannabis use days compared to TAU, and the limitations noted above, we rated the SoE for all comparative effects as **insufficient**.

Table 14. Nonbrief behavioral interventions and cannabis use days: Net mean difference of use days per month between all interventions

Intervention(s)	CBT	CBT+Fam	CBT+ICM	CBT+MI	CBT+MI+CM	CBT+MI+Fam	Educ	Fam	Fam+CM+ PeerGroup	Fam+PeerGroup	MI	PeerGroup	TAU
CBT	**CBT**	-2.9 (-11.1, 5.6)	***-6.7 (-12.7, -1)***	6.3 (-0.3, 13.3)	6.7 (-0.1, 13.7)	0.7 (-6.2, 7.7)	3.2 (-3, 9.6)	***-2.8 (-5.1, -0.3)***	-4 (-11.4, 3.8)	-4.9 (-12.5, 2.6)	-0.8 (-7.1, 5.5)	-1 (-7.4, 5.5)	***-4.2 (-7.5, -0.7)***
CBT+Fam	2.9 (-5.6, 11.1)	**CBT+Fam**	-3.9 (-14.1, 5.7)	***9.2 (0.5, 18)***	***9.5 (0.8, 18.4)***	3.6 (-5.5, 11.6)	6.1 (0.3, 11.5)	0.1 (-8.1, 8)	-1.3 (-12, 9.8)	-2.1 (-12.9, 8.6)	1.9 (-8, 11.6)	1.7 (-8.3, 11.5)	-1.3 (-10, 7)
CBT+ICM	***6.7 (1, 12.7)***	3.9 (-5.7, 14.1)	**CBT+ICM**	***13.3 (4.8, 21.9)***	***13.5 (5, 22.2)***	7.4 (-0.8, 15.9)	10.1 (2.1, 18.1)	4 (-1.3, 9.5)	2.8 (-5.5, 11.1)	1.9 (-6.1, 10)	5.9 (-0.8, 13.3)	5.7 (-1.2, 12.9)	2.6 (-2.2, 7.5)
CBT+MI	-6.3 (-13.3, 0.3)	***-9.2 (-18, -0.5)***	***-13.3 (-21.9, -4.8)***	**CBT+MI**	0.3 (-1, 1.6)	-5.7 (-13, 1.4)	-3.1 (-9.9, 3.1)	***-9.1 (-15.6, -2.9)***	-10.5 (-20.3, -0.5)	***-11.1 (-21.6, -2)***	-7.3 (-16.5, 1.3)	-7.5 (-16.9, 1.3)	***-10.5 (-17.4, -4)***
CBT+MI+CM	-6.7 (-13.7, 0.1)	***-9.5 (-18.4, -0.8)***	***-13.5 (-22.2, -5)***	-0.3 (-1.6, 1)	**CBT+MI+CM**	-6 (-13.4, 1.2)	-3.4 (-10.3, 2.9)	***-9.4 (-16.1, -3.1)***	-10.8 (-20.6, -0.8)	***-11.4 (-22, -2.2)***	-7.6 (-16.8, 1.1)	-7.8 (-17.2, 1.1)	***-10.8 (-17.8, -4.1)***
CBT+MI+Fam	-0.7 (-7.7, 6.2)	-3.6 (-11.6, 5.5)	-7.4 (-15.9, 0.8)	5.7 (-1.4, 13)	6 (-1.2, 13.4)	**CBT+MI+Fam**	2.4 (-3.9, 9.2)	-3.3 (-9.9, 3)	-4.8 (-13.8, 5.3)	-5.6 (-15, 4)	-1.5 (-9.9, 7)	-1.7 (-10.2, 6.9)	-4.8 (-11.9, 2.1)
Educ	-3.2 (-9.6, 3)	***-6.1 (-11.5, -0.3)***	***-10.1 (-18.1, -2.1)***	3.1 (-3.1, 9.9)	3.4 (-2.9, 10.3)	-2.4 (-9.2, 3.9)	**Educ**	***-5.9 (-11.9, -0.3)***	-7.4 (-16.9, 2.6)	-8.2 (-17.4, 1.2)	-4.2 (-12.4, 4.6)	-4.3 (-12.7, 4.3)	***-7.3 (-13.8, -1.2)***
Fam	***2.8 (0.3, 5.1)***	-0.1 (-8, 8.1)	-4 (-9.5, 1.3)	***9.1 (2.9, 15.6)***	***9.4 (3.1, 16.1)***	3.3 (-3, 9.9)	5.9 (0.3, 11.9)	**Fam**	-1.2 (-8.3, 6.1)	-2.1 (-9.5, 4.9)	1.9 (-4.1, 7.8)	1.7 (-4.4, 7.8)	-1.4 (-3.8, 1)
Fam+CM+ PeerGroup	4 (-3.8, 11.4)	1.3 (-9.8, 12)	-2.8 (-11.1, 5.5)	***10.5 (0.5, 20.3)***	***10.8 (0.8, 20.6)***	4.8 (-5.3, 13.8)	7.4 (-2.6, 16.9)	1.2 (-6.1, 8.3)	**Fam+CM+ PeerGroup**	-0.9 (-5.6, 4.1)	3.1 (-1.2, 7.7)	2.9 (-1.2, 7.3)	-0.2 (-7.2, 6.4)
Fam+PeerGroup	4.9 (-2.6, 12.5)	2.1 (-8.6, 12.9)	-1.9 (-10, 6.1)	***11.1 (2, 21.6)***	***11.4 (2.2, 22)***	5.6 (-4, 15)	8.2 (-1.2, 17.4)	2.1 (-4.9, 9.5)	0.9 (-4.1, 5.6)	**Fam+PeerGroup**	4 (-0.2, 8.3)	3.8 (-0.2, 7.9)	0.7 (-5.9, 7.5)
MI	0.8 (-5.5, 7.1)	-1.9 (-11.6, 8)	-5.9 (-13.3, 0.8)	7.3 (-1.3, 16.5)	7.6 (-1.1, 16.8)	1.5 (-7, 9.9)	4.2 (-4.6, 12.4)	-1.9 (-7.8, 4.1)	-3.1 (-7.7, 1.2)	-4 (-8.3, 0.2)	**MI**	-0.2 (-1.6, 1.2)	-3.3 (-8.6, 1.9)
PeerGroup	1 (-5.5, 7.4)	-1.7 (-11.5, 8.3)	-5.7 (-12.9, 1.2)	7.5 (-1.3, 16.9)	7.8 (-1.1, 17.2)	1.7 (-6.9, 10.2)	4.3 (-4.3, 12.7)	-1.7 (-7.8, 4.4)	-2.9 (-7.3, 1.2)	-3.8 (-7.9, 0.2)	0.2 (-1.2, 1.6)	**PeerGroup**	-3.1 (-8.6, 2.3)
TAU	***4.2 (0.7, 7.5)***	1.3 (-7, 10)	-2.6 (-7.5, 2.2)	***10.5 (4, 17.4)***	***10.8 (4.1, 17.8)***	4.8 (-2.1, 11.9)	7.3 (1.2, 13.8)	1.4 (-1, 3.8)	0.2 (-6.4, 7.2)	-0.7 (-7.5, 5.9)	3.3 (-1.9, 8.6)	3.1 (-2.3, 8.6)	**TAU**

Bold font indicates the 95% CrI for the comparative effect excludes the null effect.

Abbreviations: CBT = cognitive behavioral therapy; CM = contingency management; Educ = psychoeducation; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; TAU = treatment as usual.

These patterns are reflected in the rankings, Table 15, which estimates that TAU has a 79 percent chance of being in the top third of all interventions.

Table 15. Probabilities of nonbrief behavioral interventions ranking in top third, middle third and bottom third to reduce cannabis use days

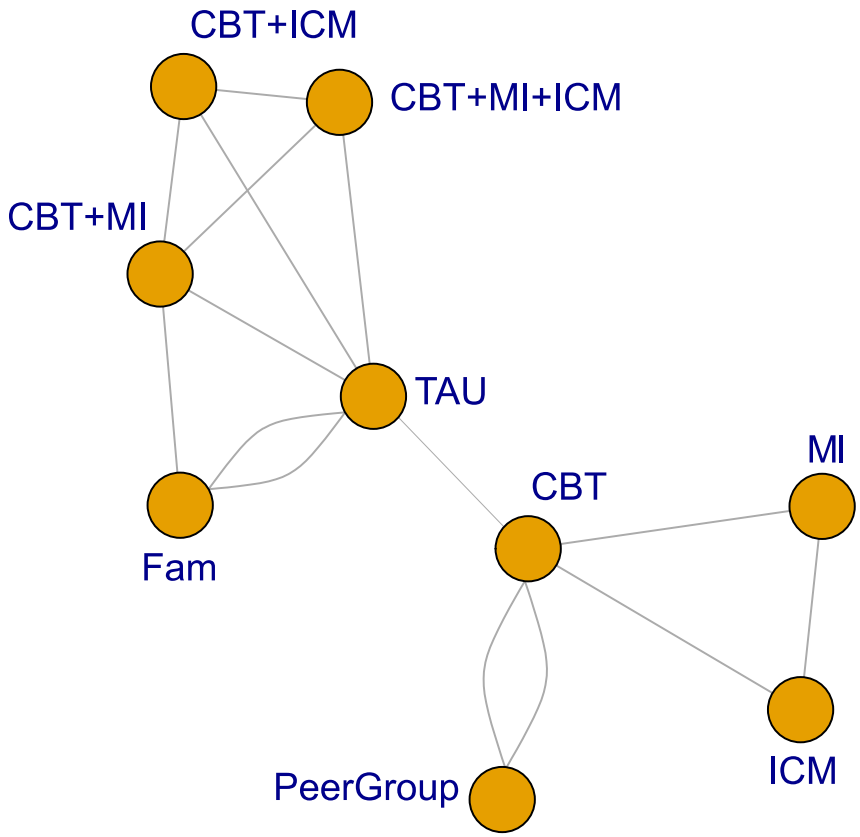
Intervention(s)	SUCRA	Top Third	Middle Third	Bottom Third
CBT+ICM	91%	91	8	1
Fam+PeerGroup	81%	71	26	3
TAU	79%	72	28	0
Fam+CM+PeerGroup	74%	59	33	8
Fam	66%	33	64	2
CBT+Fam	66%	44	32	24
PeerGroup	51%	10	59	30
MI	48%	5	59	36
CBT	44%	2	46	52
CBT+MI+Fam	43%	10	30	60
Educ	27%	1	12	87
CBT+MI	17%	0	2	98
CBT+MI+CM	12%	0	1	99

Abbreviations: CBT = cognitive behavioral therapy; CM = contingency management; Educ = psychoeducation; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; SUCRA = surface area under the cumulative ranking curve; TAU = treatment as usual

Alcohol and Other Drug Use

Eight studies reported aggregate use days for alcohol and other drugs by 1,202 participants, with comparisons illustrated in Figure 23.[112, 119, 127, 139, 141, 142, 162, 189, 194, 195] One of these studies, with 32 subjects, reported a scale that reflected aggregate alcohol and drug use.[141, 142] There were six dual-arm studies and two multi-arm studies.

Figure 23. Evidence graph for studies reporting aggregate alcohol and other drug use days

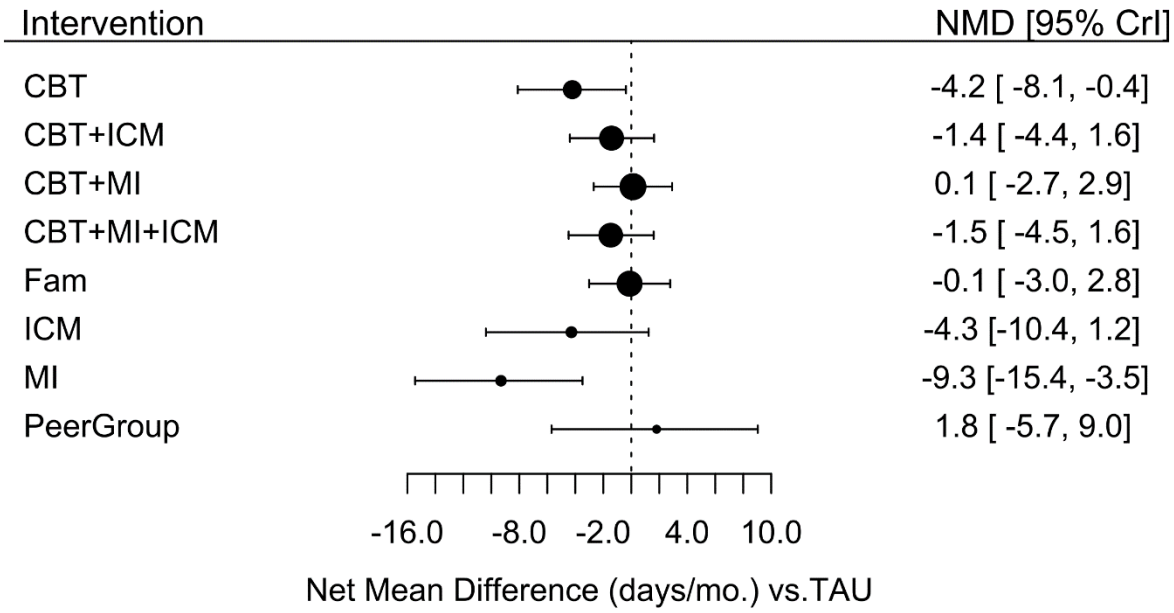


Key Question 1: Aggregate Alcohol and Other Drug Use — Behavioral Interventions Compared to TAU

Overall the precision of estimates was low (Figure 24). This network is very sparse and loosely connected, and because most RCTs are small, the statistical power to detect inconsistency between direct and indirect effects is very limited. Estimates of treatment effectiveness are very imprecise.

Of the interventions compared, MI and CBT were more effective than TAU. We rated the associated SoE as **low**.

Figure 24. Aggregate alcohol and other drug use: Summary forest plot of meta-analyzed net mean differences for all interventions compared with TAU



NMD < 1 favors intervention versus TAU. Abbreviations: MI = motivational interviewing; Fam = family focused therapy; CBT = cognitive behavioral therapy; CM = contingency management; PeerGroup = peer group therapy; ICM = intensive case management; TAU = treatment as usual; CrI = credible interval

Key Question 2: Aggregate Alcohol and Other Drug Use — Comparative Effects of Behavioral Interventions

Table 16 details the comparative effects the studied interventions in studies reporting aggregate alcohol and other drug use outcomes. When the interventions are ranked, MI has the highest probability (0.98) of ranking in the top third (Table 17). Most of the results in the Table are based on indirect data, with direct data limited to only one or two studies. The statistical power to detect inconsistency between direct and indirect effects is very limited. Thus, estimates of treatment effectiveness are very imprecise.

MI was more effect than CBT+MI, Fam, and CBT. We rated the associated SoE as **low**.

Table 16. Nonbrief behavioral interventions and aggregate alcohol and other drug use: Net mean difference of use days per month between all interventions

Intervention(s)	CBT	CBT+ICM	CBT+MI	CBT+MI+ICM	Fam	ICM	MI	PeerGroup	TAU
CBT	**CBT**	2.8 (-2.1, 7.9)	4.3 (-0.4, 9.2)	2.7 (-2.2, 7.7)	4.1 (-0.8, 8.9)	-0.2 (-4.7, 4.1)	**-5.2** **(-9.7, -0.8)**	6 (-0.1, 12.2)	4.2 (0.4, 8.1)
CBT+ICM	-2.8 (-7.9, 2.1)	**CBT+ICM**	1.5 (-1.3, 4.3)	-0.1 (-3, 2.7)	1.2 (-2.8, 5.2)	-3 (-9.7, 3.4)	**-8** **(-14.9, -1.3)**	3.2 (-4.9, 10.9)	1.4 (-1.6, 4.4)
CBT+MI	-4.3 (-9.2, 0.4)	-1.5 (-4.3, 1.3)	**CBT+MI**	-1.6 (-4.4, 1.1)	-0.3 (-3.9, 3.4)	-4.4 (-10.9, 1.8)	**-9.5** **(-16.1, -3)**	1.7 (-6.4, 9.4)	-0.1 (-2.9, 2.7)
CBT+MI+ICM	-2.7 (-7.7, 2.2)	0.1 (-2.7, 3)	1.6 (-1.1, 4.4)	**CBT+MI+ICM**	1.3 (-2.7, 5.3)	-2.9 (-9.5, 3.4)	**-7.8** **(-14.8, -1.3)**	3.3 (-4.8, 11.2)	1.5 (-1.6, 4.5)
Fam	-4.1 (-8.9, 0.8)	-1.2 (-5.2, 2.8)	0.3 (-3.4, 3.9)	-1.3 (-5.3, 2.7)	**Fam**	-4.2 (-10.8, 2.1)	**-9.3** **(-15.8, -2.7)**	1.9 (-6.1, 9.8)	0.1 (-2.8, 3)
ICM	0.2 (-4.1, 4.7)	3 (-3.4, 9.7)	4.4 (-1.8, 10.9)	2.9 (-3.4, 9.5)	4.2 (-2.1, 10.8)	**ICM**	**-5** **(-9.3, -0.7)**	6.1 (-1.1, 13.9)	4.3 (-1.2, 10.4)
MI	**5.2** **(0.8, 9.7)**	8 (1.3, 14.9)	9.5 (3, 16.1)	7.8 (1.3, 14.8)	9.3 (2.7, 15.8)	5 (0.7, 9.3)	**MI**	11.3 (3.6, 18.7)	9.3 (3.5, 15.4)
PeerGroup	-6 (-12.2, 0.1)	-3.2 (-10.9, 4.9)	-1.7 (-9.4, 6.4)	-3.3 (-11.2, 4.8)	-1.9 (-9.8, 6.1)	-6.1 (-13.9, 1.1)	**-11.3** **(-18.7, -3.6)**	**PeerGroup**	-1.8 (-9, 5.7)
TAU	**-4.2** **(-8.1, -0.4)**	-1.4 (-4.4, 1.6)	0.1 (-2.7, 2.9)	-1.5 (-4.5, 1.6)	-0.1 (-3, 2.8)	-4.3 (-10.4, 1.2)	**-9.3** **(-15.4, -3.5)**	1.8 (-5.7, 9)	**TAU**

Bold font indicates the 95% CrI for the comparative effect excludes the null effect.

Abbreviations: CBT = cognitive behavioral therapy; CM = contingency management; Educ = psychoeducation; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; TAU = treatment as usual

Table 17. Probabilities of nonbrief behavioral interventions ranking in top third, middle third and bottom third to reduce aggregate alcohol and other drug use days

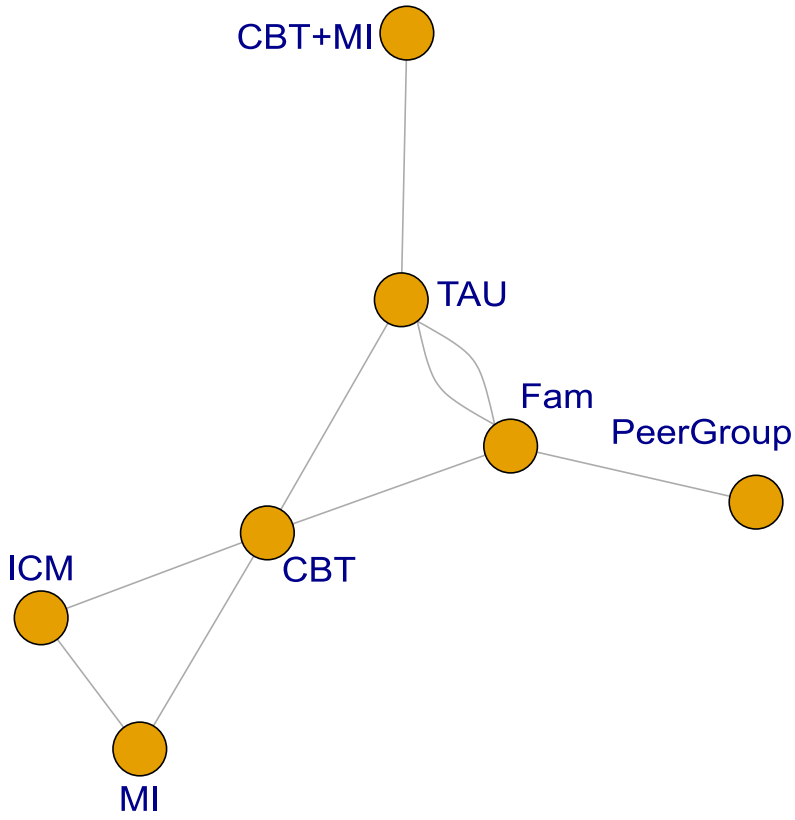
Intervention(s)	SUCRA	Top Third	Middle Third	Bottom Third
MI	99%	100	0	0
CBT	79%	83	15	2
ICM	76%	75	18	7
CBT+MI+ICM	58%	17	68	14
CBT+ICM	56%	15	67	18
Fam	37%	4	37	58
TAU	36%	0	38	61
CBT+MI	34%	2	34	65
PeerGroup	26%	4	22	74

Abbreviations: CBT = cognitive behavioral therapy; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; SUCRA = surface area under the cumulative ranking curve; TAU = treatment as usual

Illicit Drug Use Outcomes

Five studies with 1,310 participants[113, 174-181, 190, 206, 207, 210] reported illicit drug use days, and two studies with 281 participants[153, 205] reported a scale reflecting illicit drug use. These compare interventions as shown in Figure 25.

Figure 25. Evidence graph for studies reporting illicit drug use days



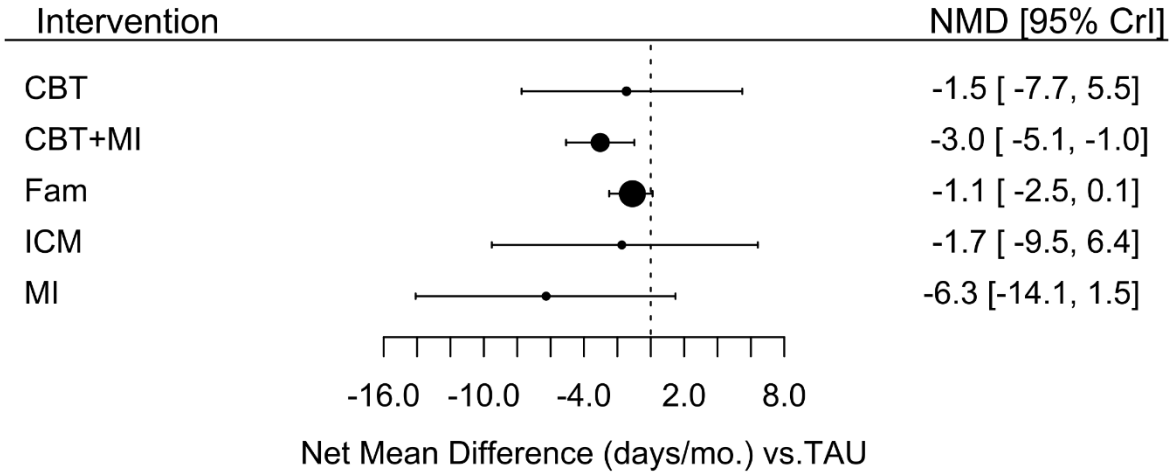
Abbreviations: Fam = family; CM = contingency management; TAU = treatment as usual; CBT = cognitive behavioral therapy; ICM = intensive case management; MI = motivational interviewing; Educ = education.

Key Question 1: Illicit Drug Use Days — Interventions Compared to TAU

CBT+MI resulted in a net decrease in overall illicit drug use days, compared to TAU. We rated the associated SoE as **low**.

The effects for CBT, ICM and MI were imprecisely estimated, as illustrated in Figure 26. This network is also very sparse and loosely connected, and because most RCTs are small, the statistical power to detect inconsistency between direct and indirect effects is very limited. Estimates of treatment effectiveness are very imprecise.

Figure 26. Illicit drug use days: Summary forest plot of interventions reporting meta-analyzed illicit drug use days compared to TAU



Abbreviations: Fam = family; CM = contingency management; TAU = treatment as usual; CBT = cognitive behavioral therapy; ICM = intensive case management; MI = motivational interviewing; Educ = education.

Key Question 2: Illicit Drug Use Days — Comparative Effects

None of the active interventions or combined interventions were different from each other (Table 18). We rated the associated SoE as **insufficient**.

Most of the results in the Table are based on indirect data, with direct data limited to only one or two studies. The statistical power to detect inconsistency between direct and indirect effects is very limited. Thus, estimates of treatment effectiveness are very imprecise.

As shown in Table 19, MI was most likely to rank in the top third. TAU had a 75 percent probability of ranking in the bottom third.

Table 18. Nonbrief behavioral interventions and illicit drug use: Net mean difference of use days per month between all interventions

Intervention(s)	CBT	CBT+MI	Fam	ICM	MI	TAU
CBT	**CBT**	-1.6 (-8.8, 5.1)	0.3 (-6.5, 6.5)	-0.2 (-4.8, 4)	***-4.9 (-9.5, -0.4)***	1.5 (-5.5, 7.7)
CBT+MI	1.6 (-5.1, 8.8)	**CBT+MI**	1.9 (-0.5, 4.2)	1.3 (-6.7, 9.6)	-3.2 (-11.3, 4.7)	3 (1, 5.1)
Fam	-0.3 (-6.5, 6.5)	-1.9 (-4.2, 0.5)	**Fam**	-0.6 (-8.3, 7.4)	-5.1 (-12.8, 2.5)	1.1 (-0.1, 2.5)
ICM	0.2 (-4, 4.8)	-1.3 (-9.6, 6.7)	0.6 (-7.4, 8.3)	**ICM**	***-4.6 (-9, -0.2)***	1.7 (-6.4, 9.5)
MI	4.9 (0.4, 9.5)	3.2 (-4.7, 11.3)	5.1 (-2.5, 12.8)	4.6 (0.2, 9)	**MI**	6.3 (-1.5, 14.1)
TAU	-1.5 (-7.7, 5.5)	***-3 (-5.1, -1)***	-1.1 (-2.5, 0.1)	-1.7 (-9.5, 6.4)	-6.3 (-14.1, 1.5)	**TAU**

Bold font indicates statistical significance.

Abbreviations: CBT = cognitive behavioral therapy; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; TAU = treatment as usual

Table 19. Probabilities of nonbrief behavioral interventions ranking in top third, middle third and bottom third to reduce illicit drug use days

Intervention(s)	SUCRA	Top Third	Middle Third	Bottom Third
MI	**93%**	**90**	**9**	**1**
CBT+MI	74%	55	42	3
ICM	53%	30	31	39
Fam	50%	10	46	44
CBT	50%	14	47	39
TAU	**29%**	**0**	**25**	**75**

Bold font indicates the highest probability of ranking in top third and bottom third respectively.

Abbreviations: CBT = cognitive behavioral therapy; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; SUCRA = surface area under the cumulative ranking curve; TAU = treatment as usual

Other Outcomes

Other outcomes were sparsely reported. The outcomes, number of studies reporting the outcome and number of participants are summarized in Table 20 below.

Table 20. Other outcome participant summaries

Outcome	No. Studies	No. Participants
School Performance and Educational Attainment	5[113, 141, 143, 154, 187]	353
Family Related	5[141, 143, 154, 174, 185]	709
Peer Related	3[141, 143, 154]	200
Mental Health Events	2[121, 146]	184
Physical Health Events	2[121, 184]	194
Legal Outcomes*	10[113, 119, 121, 130, 135, 139, 141, 143, 187, 208]	1620

*Legal outcomes include arrests and convictions, self-reported general delinquency/illegal behavior, self-reported crimes against persons and property crimes/theft.

These studies evaluated multiple interventions using a variety of outcome metrics. In general, estimated effects were imprecise with no clear trends across studies. Study-specific details are tabulated in Appendix G (Tables G-4 to G-8).

Systematic Reviews of Treatments for Alcohol Use in the College Setting

Key Points

- 2 SRs of the general population of college students who drink alcohol found that, on average, compared to no intervention, behavioral interventions resulted in reduced alcohol use for up to about 6 months, but these effects waned in the long term. However, behavioral interventions resulted in fewer alcohol-related problems over the medium to long term. One SR found that, by indirect comparison, face-to-face interventions provide larger and more enduring effects than computer-delivered interventions (SOE not assessed).
- 2 SRs focused on college students mandated to attend alcohol programs. On average, alcohol use decreased in the short- to medium-term regardless of intervention, but mostly did not persist. Four specific commercially available interventions were found to be more effective in the short term than others (SOE not assessed).
- 2 SRs focused on college students who engaged in heavy or hazardous alcohol use. Brief, single-session interventions and the commercially-available BASICS program were found to reduce alcohol use compared with no intervention. Among the brief behavioral interventions, MET/MI had the strongest effect (SOE not assessed).

To evaluate treatment of alcohol use disorders/problematic alcohol use in the college setting, we summarized existing SRs only, since this literature is large, highly contextual, and has been extensively reviewed. The search for SRs addressing interventions for treating problematic alcohol use or alcohol use disorder in the college setting identified six SRs published between 2005 and 2015. These SRs included between 16 and 73 studies each (median 40).

The SRs mostly meta-analyzed standardized effect sizes across multiple outcomes and interventions. This approach requires the strong (and unlikely) assumption that effects are homogeneous across disparate outcomes and interventions. In general these SRs did not adequately perform and report risk of bias assessments and did not discuss the consistency of results. Given these limitations, we have not make SoE assessments.

General Population of College Students Who Drink Alcohol

Two SRs did not require any population-specific eligibility criteria for studies other than that the study participants be college students who consume alcohol.[211, 212]

Carey 2007 reported a SR of 62 randomized controlled trials (RCTs), with 13,750 participants that compared 98 separate individual-level behavioral interventions (usually multicomponent) with control interventions.[211] Studies included different subpopulations, such as heavy drinkers, moderate drinkers, and alcohol offenders. Effect sizes (standardized mean differences) were reported in the immediate term (≤3 weeks), short term (4 to 13 weeks), intermediate term (14 to 26 weeks), and long term (27 to 195 weeks) for various alcohol use measures and alcohol-related problem measures. The meta-analyses were deemed inadequate due to use of effect sizes comprised of disparate outcomes, inclusion of multiple effect sizes from individual studies, and exclusion of outlier results.

The effect sizes for the alcohol use measures (e.g., alcohol use quantity, frequency of heavy drinking) generally favored the intervention groups until the intermediate term, ranging from 0.11 to 0.41 standard deviation (SD) units. However, these benefits did not persist in the long term; almost all effect sizes diminished over time. In the long term, the only persistent effect of the interventions on alcohol use was on frequency of drinking days (effect size=0.16 SD units, 95% CI 0.03 to 0.30).

A different pattern emerged for the alcohol-related problem measures (e.g., drinking and driving, property damage, fights). Although students in the intervention groups had fewer alcohol-related problems than those in the control groups, the beneficial effect of the interventions on alcohol-related problem measures took longer to emerge (no immediate effect, but short-term effect size=0.15 SD units, 95% CI 0.08 to 0.21), peaked in the intermediate term (effect size=0.22 SD units, 95% CI 0.12 to 0.32), and persisted in the long term (effect size=0.14 SD units, 95% CI 0.06 to 0.22).[211]

In a subsequent SR, Carey 2012 primarily examined RCTs (47 RCTs, 1 nonrandomized comparative study [NRCS]), with 5,237 participants, that focused on the mode of delivery of behavioral interventions.[212] The SR compared face-to-face interventions and computer-delivered behavioral interventions with TAU or no intervention, and with each other. Carey 2012 examined similar outcomes as Carey 2007 that were analyzed using the same effect size measurements at the same follow-up time-periods. The meta-analyses, thus, had similar issues as Carey 2007, except that outlier results were not omitted.

Compared with TAU, students receiving face-to-face interventions drank less per week or month (effect sizes ranged from 0.15 to 0.19 SD units) and per drinking day (effect sizes ranged from 0.17 to 0.23 SD units), drank less frequently (effect sizes ranged from 0.07 to 0.16 SD units), and reported fewer alcohol-related problems (effect sizes ranged from 0.09 to 0.15 SD units) in the short and intermediate term. However, the only persistent effect of face-to-face interventions in the long term was on alcohol use per drinking day (effect size=0.16, 95% CI 0.03 to 0.30 SD units).

Comparing different active interventions, students in the computer-delivered interventions groups had similar benefits as face-to-face interventions in the short term (4 to 13 weeks), but not in the intermediate or long term. Direct comparisons between face-to-face interventions and computer-delivered interventions were infrequent. In the short term, the two modes of delivery had similar effects on alcohol use and alcohol-related problems. However, face-to-face interventions were more effective in reducing peak blood alcohol concentration (BAC) in the intermediate term (weighted sum of squares of group mean effect size [Q_b]=6.74, p=0.009) and frequency of heavy drinking in the long term (Q_b=6.65, p=0.010). Overall, Carey 2012 concluded that face-to-face interventions provide the strongest and most enduring effects in this population.[212]

College Students Mandated To Receive Interventions for Alcohol Use

Two SRs focused on studies of college students who were mandated to attend a program to reduce their alcohol consumption.[213, 214]

Carey 2016 included 31 studies (21 RCTs and 10 NRCSs), with 8,621 participants, that compared various group- or individual-level behavioral treatments. A single effect size was selected from each study for inclusion in meta-analysis, but the effect sizes were comprised of disparate outcomes.

In the short term (i.e., ≤13 weeks), all alcohol use and alcohol-related problem measures improved (compared with baseline) in students, regardless of interventions (within-group effect sizes ranged from 0.14 to 0.27 SD units). In the medium term, improvements were observed in frequency of heavy drinking (effect size=0.14 SD units, 95% CI 0.04 to 0.23), peak BAC (effect size=0.25 SD units, 95% CI 0.14 to 0.36), typical BAC (effect size=0.17 SD units, 95% CI 0.04 to 0.29), and alcohol-related problems (effect size=0.13 SD units, 95% CI 0.06 to 0.21). However, the only within-group effect to persist in the long term was on typical BAC (effect size=0.12 SD units, 95% CI 0.01 to 0.25).

Four commercially available intervention protocols (Brief Alcohol Screening and Intervention for College Students [BASICS], Electronic Check-Up To Go [e-CHUG], Alcohol 101, and Alcohol Skills Training Program) were shown to be most effective. Carey 2016 reported between-group comparisons, based on short term followup, when one of these 4 interventions was mandated. In the control group, participation in a mandated intervention was associated with lower number of drinks per week (between-group effect size=0.13 SD units, 95% CI 0.02 to 0.25), peak BAC (effect size=0.20 SD units, 95% CI 0.06 to 0.33**)**, and typical BAC (effect size=0.16 SD units, 95% CI 0.01 to 0.31). Alcohol-related problems were similar between the two groups.[214]

Barnett 2005 included 16 studies, but only three of these, all RCTs with a total of 213 participants, were comparative in design.[213] Due to small numbers of similar studies, meta-analysis was not performed. The three trials randomized mandated college students to three pairs of brief behavioral interventions (MI vs. alcohol education, lifestyle management compared to no intervention, and videotaped expectancy challenge vs. alcohol education). Outcomes were similar and not statistically significant for the first two comparisons/studies, except that MI was more effective than alcohol education in improving alcohol-related problems (between-group effect size=0.39 SD units, $p<0.05$). For the third comparison/study, alcohol education was more effective than the alcohol expectancy challenge intervention in improving alcohol knowledge (effect size=−1.47 SD units, $p<0.05$).[213]

College Students Who Engaged in Heavy or Hazardous Levels of Alcohol Use

Two SRs examined studies of college students who engaged in heavy or hazardous levels of alcohol use.[215, 216] Both SRs focused on the comparison between brief behavioral interventions (one or two sessions) with no intervention or TAU.

Samson 2015 included 73 studies ("experimental" or "controlled quasi-experimental" studies) that evaluated a single-session intervention (CBT, MET/MI, personalized feedback, or psychoeducation therapy [PET]).[216] The meta-analysis combined 662 disparate effect sizes from 73 individual studies. The total number of participants was not reported.

Single-session interventions were found to have a modest effect on reducing alcohol consumption among heavy-drinking college students (effect size=0.18 SD units, 95% CI 0.12 to 0.24). Among the various types of single-session interventions, MET/MI was found to

have the strongest effect. This suggests that single-session interventions that incorporate aspects of MET/MI are likely the most effective among the single-session interventions in this population.[216]

Fachini 2012 included 18 RCTs, with a total of 6,233 participants, that compared BASICS with TAU or no intervention in students engaged in heavy episodic drinking.[215] The meta-analyses focused on specific outcomes, and were deemed to be adequate. Overall, BASICS lowered both alcohol consumption and negative consequences in college students. Compared with the control group, students who received BASICS had fewer drinks per week (mean difference = −1.50, 95% CI −3.24 to −0.29) and fewer alcohol-related problems measured using the Rutgers Alcohol Program Index (RAPI) (mean difference in score = −0.87, 95% CI −1.58 to −0.20).

Risk of Bias

Based on a modified AMSTAR 2 assessment (Table 21), the SRs mostly adhered to standard design and reporting elements (except for failure to report methods regarding screening citations and articles). Four of the five SRs that conducted meta-analyses were deemed to have used inappropriate methods, only one SR adequately evaluated the summary results based on risk of bias assessments, and only one study reported conflict of interest information (they reported none). The primary concern about the meta-analyses, was that SRs mostly combined standardized effect sizes comprised of disparate sets of outcomes and often included multiple effect sizes from individual studies.

Table 21. Risk of bias in college alcohol intervention systematic reviews

Author Year PMID	PICOD[a]	Lit Search[b]	Dupl Screen[c]	Dupl Extrn[d]	Study Details[e]	RoB[f]	MA[g]	RoB Analysis[h]	Heterogeneity[i]	COI[j]
Barnett 2005 16135343	Sufficient	Yes	NR	NR	Sufficient[k]	No	N/A	No	No	No
Carey 2007 17590277	Yes	Yes	NR	Yes	Yes	No	No[L]	No	Yes	No
Fachini 2012 22967716	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No[m]	Yes
Carey 2012 23022767	Yes	Yes	NR	Yes	Yes	Sufficient[n]	No[o]	Yes	Yes	No
Samson 2015 26098028	Yes	Yes	Yes	Yes	No	Sufficient[p]	No[q]	No	Yes	No
Carey 2016 27100126	Yes	Yes	NR	Yes	Yes	Sufficient[r]	No[s]	No[t]	Yes	No

Ratings based on AMSTAR 2. Ratings: Yes = item explicitly reported (or done), No = item not reported (or done), Sufficient = reporting of item was adequate but not fully explicit, NR = not reported, N/A = not applicable. Ratings are color coded for emphasis only. Other abbreviations are defined in the footnotes.

a Did the research questions and inclusion criteria for the review include the components of PICOD (population, intervention, comparator, outcomes, study design)? (AMSTAR 2 item 1)
b Did the review authors use a comprehensive literature (Lit) search strategy? (AMSTAR 2 item 4)
c Did the review authors perform study selection (Screen) in duplicate (Dupl)? (AMSTAR 2 item 5)
d Did the review authors perform data extraction (Extrn) in duplicate (Dupl)? (AMSTAR 2 item 6)
e Did the review authors describe the included studies in adequate detail? (AMSTAR 2 item 8)
f Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? (AMSTAR 2 item 9)
g If meta-analysis (MA) was performed did the review authors use appropriate methods for statistical combination of results? (AMSTAR 2 item 11) See subsequent footnotes. Meta-analyses of standardized effect sizes pertaining to disparate outcomes were not deemed to be appropriate for statistical combination.
h Did the review authors assess the potential impact of risk of bias (RoB) in individual studies on the summary results, interpretation, discussion? (AMSTAR 2 item 13)
i Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? (AMSTAR 2 item 14)
j Did the review authors report any potential sources of conflict of interest (COI) regarding conducting the review? (AMSTAR 2 item 16)
k Populations of included studies were not well described
l Multiple effect sizes within studies were averaged prior to meta-analysis. In addition, outliers were excluded from meta-analysis.
m Moderators of effect were included in the discussion, but only qualitatively.

n A risk of bias score (range 0−17) was used, but not adequately described.
o Multiple effect sizes within studies were averaged prior to meta-analysis.
p Risk of bias assessment was unclear and possibly incomplete.
q 662 effect sizes from 73 studies were included in a single meta-analysis.
r Unclear, possibly incomplete, risk of bias assessment.
s A single effect size was selected from each study for meta-analysis, but effect sizes pertained to disparate outcomes.
t Meta-analyses were adjusted for risk of bias, but not analyzed based on risk of bias.

Pharmaceutical Interventions

We found only a small number of studies pharmacologic treatments (with or without combined behavioral interventions) for substance use disorder in adolescents. We found no large nonrandomized studies which evaluated medication side-effects in adolescents.

In studies that combined pharmacologic and behavioral interventions, the behavioral interventions were often less completely described, and therefore not easily compared to the detailed manual based interventions typical in behavioral trials. Drug trials included placebo arms, which due to the likelihood of a placebo effect, were not deemed comparable to TAU arms in studies of behavioral interventions. Thus, we did not jointly synthesize studies of behavioral interventions with studies of pharmacologic interventions and summarize these studies separately by use disorder.

Key Points

- Opioid use disorder
  - Longer courses (2 to 3 months) of buprenorphine are more effective than shorter courses (14 to 28 days) to reduce opioid use and achieve abstinence (**low** SoE)
    - Buprenorphine-naloxone (12-week versus 2-week) is more effective in reducing opioid use at 9 and 12 months (1 study)
    - Buprenorphine+CBT+CM was more effective than clonidine+CBT+CM in increasing odds of opioid abstinence at 1 month (1 study)

Opioid Use Disorder

Four comparative studies (in 13 publications[217-228]) published between 2005 and 2016 assessed pharmacologic or combination pharmacologic and behavioral interventions to reduce opioid use in a total of 330 adolescents, all of whom had SUD. Participants in the studies were on average 17 to 23 years of age (range across studies 14 to 25 years). Baseline and arm details are given in Table 22. Risk of Bias summaries are given in Figure 27.

Table 22. Baseline data and Interventions: Pharmacologic interventions for opioid use

Author, Year	N	Substances Used	Severity	Ages [Eligible] Mean (SD)	Male %	Setting	Intervention Delivery	Arm Names
Gonzalez, 2015[219, 229]	87	opioid cannabis	SUD	[18, 25] 22.6 (1.9)	66	outpatient research clinic	research staff (PhD psychologist)	1. Buprenorphine-Naloxone+Placebo+CBT (group): "Placebo" 2. Buprenorphine-Naloxone+Memantine30+CBT (group): "Memantine 30" 3. Buprenorphine-Naloxone+Memantine15+CBT (group): "Memantine 15"

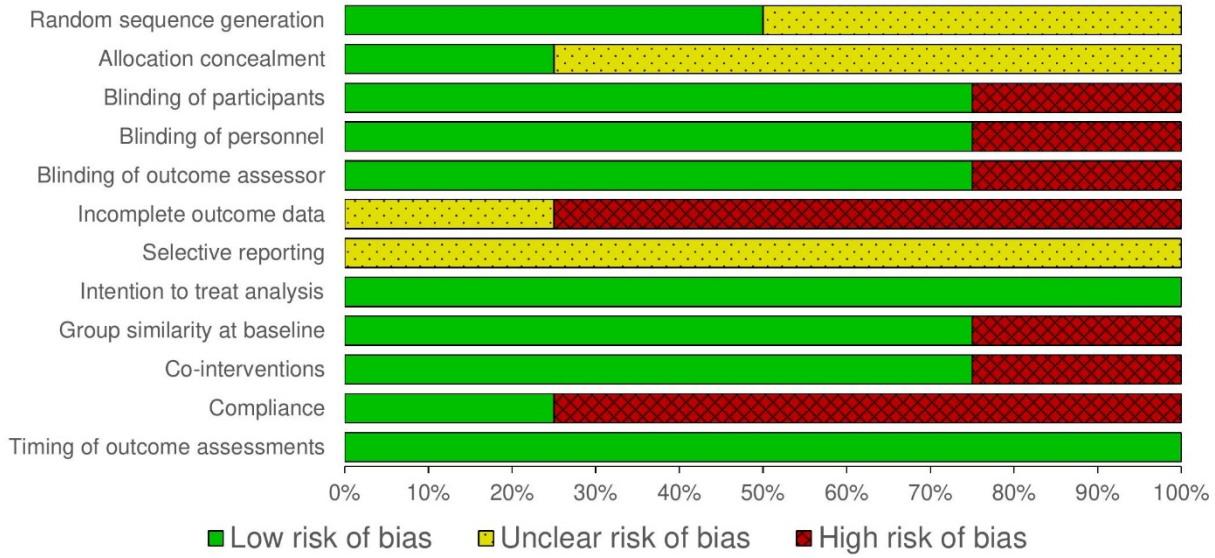
Author, Year	N	Substances Used	Severity	Ages [Eligible] Mean (SD)	Male %	Setting	Intervention Delivery	Arm Names
Marsch, 2005[221, 224]	36	opioid cannabis alcohol cocaine amphetamine	SUD	[13, 18] 17.3 (0.7)	50	outpatient research clinic	no detail (drug trial)	1. Clonidine+CBT+CM: "Clonidine" 2. Buprenorphine+CBT+CM: "Buprenorphine"
Marsch, 2016[222]	53	opioid alcohol cocaine cannabis amphetamine	SUD	[16, 24] 21 (2.5)	54	outpatient research clinic	no detail (drug trial)	1. Buprenorphine+Placebo+ CBT+MI+Educ+ Fam[systems/structural]+CM: "Buprenorphine 28-day taper" 2. Buprenorphine+CBT+MI+ Educ+Fam[systems/structural]+ CM: "Buprenorphine 56-day taper"
Woody, 2008[217, 218, 220, 223, 225-228]	154	opioid cannabis alcohol cocaine injection drugs	SUD	[14, 21] nr	nr	outpatient community	no detail (drug trial)	1. Buprenorphine+Naloxone-short+TAU (group): "Short-term buprenorphine-naloxone" 2. Buprenorphine+Naloxone-extended+TAU (group): "Extended buprenorphine-naloxone"

Abbreviations: CBT = cognitive behavioral therapy; CM = contingency management; ED = emergency department; Educ = psychoeducation; Fam = Family therapy; MI = motivational interviewing; N=number randomized; nr = not reported; SD = standard deviation; SUD = substance use disorder; TAU = treatment as usual

Arm names = Intervention codes, (intervention modifiers) and [family subclassification]: "study arm name".

Except for Woody 2008, the studies were double blinded. However, studies mostly had high attrition rates and poor compliance, reflecting the challenges of engaging this population.

Figure 27. Pharmacologic intervention studies for opioid use: Percentage of studies in each risk of bias category



As shown in Table 23, all four studies assessed buprenorphine-naloxone or buprenorphine alone or combined with behavioral interventions. Comparisons were between doses or tapering schedules, with clonidine, or with memantine.

Woody et al. 2008 reported that adolescents in the extended 12-week buprenorphine-naloxone arm were more likely to report no opioid use in the last month at 9 and 12 months than adolescents in the short term (2 week) buprenorphine-naloxone group, but not at 6 months. Additionally, they report an overall group-by-time interaction odds ratio for any opioid use of 1.34 (95% CI 0.70 to 2.57), favoring the extended 12-week buprenorphine-naloxone arm.[217, 218, 220, 223, 225-228]

Woody et al. 2008 reported no serious adverse events and no loss to follow-up due to adverse events. Adverse events reported were nausea, insomnia, stomach ache, vomiting, and anxiety.[217, 218, 220, 223, 225-228] A secondary analysis found that overall in the sample, those in the buprenorphine arm had a statistically significant decrease in injection drug use compared to the detox arm although there was a decrease in both groups.[223, 225]

Marsch et al. 2016 found that among those treated with buprenorphine (in combination with other behavioral interventions), opioid abstinence was higher in the 56-day taper group than in the 28-day taper group (OR 2.59, 95% CI 0.73 to 9.18).[222] They reported that there were no serious adverse events related to treatment in either arm.

Marsch et al. 2005 found that buprenorphine (combined with CBT + CM) performed better for abstinence than clonidine (combined with CBT + CM) (OR 4.00, 95% CI 1.00 to 16.0), although the confidence interval was very wide. HIV risk behavior did not differ between the groups. No information was given on adverse events.[221, 224] A secondary analysis focused on emotional and behavioral outcomes found that among youth who were retained in treatment, there were significant reductions in two grouping scales (internalizing problems and total problems) and four syndrome scales (somatic, social, attention, and thought[224]). Of note, there were more youth retained in the buprenorphine arm retained (n=13) compared to the clonidine arm (n=7).

Gonzales et al. 2015 evaluated buprenorphine-naloxone plus memantine (either 15 mg or 30 mg) or buprenorphine-naloxone plus placebo in 80 18- to 25-year-old young adults. Each arm also received weekly CBT delivered in a group format. They reported that for abstinence at 3 months, the arm with buprenorphine-naloxone plus 30 mg of memantine performed much better than the 15 mg arm (OR 9.2, 95% CI 2.62 to 32.28) or the placebo arm (OR 9.2, 95% CI 2.69 to 31.46), and the 15 mg arm performed slightly worse than placebo (OR 0.78, 95% CI 0.27 to 2.31). The same general pattern held for opioid use frequency, though the confidence intervals were wide for both abstinence and use outcomes and the 15 mg arm had a lower use frequency than placebo. Reported adverse events included pain, drowsiness, vivid dreams, constipation, upper respiratory infection, nausea, and headaches. Any adverse event was reported in 39 and 30 percent of the memantine 30 mg and 15 mg arms, respectively, as compared to 49 percent of the placebo arms, and there were no serious adverse events.[219]

Table 23. Results: Pharmacologic interventions for opioid use disorder

Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI)
Woody, 2008[217, 218, 220, 223, 225-228]	Buprenorphine + Naloxone + extended (group)	Buprenorphine + Naloxone + short (group)	Abstinence per 30 days (n, %)	1	47	13 (28)	46	17 (37)	OR 0.7 (0.3, 1.6)
			Abstinence per 30 days (n, %)	2	45	21 (47)	45	14 (30)	OR 2.0 (0.9, 4.9)
			Abstinence per 30 days (n, %)	3	49	23 (47)	42	12 (28)	**OR 2.4 (1.0, 5.8)**
			Serious adverse events	3	78	0	74	0	No events
Marsch, 2016 [222]	Buprenorphine + CBT + MI + Educ + CM (56 day taper)	Buprenorphine + Placebo + CBT + MI + Educ + CM (28 day taper)	Mean Opioid negative urine screens/28 days (mean%, 95% CI)	2	25	34.6 (23.2, 50.0)	28	17.2 (5.8, 28.6)	**Cohen's d 0.57 (0.02, 1.13)**
			Serious adverse events	2	25	0	28	0	No events
Marsch, 2005 [221, 224]	Buprenorphine + CBT + CM	Clonidine + CBT + CM	Abstinence (n, %)	1	18	12 (64)	18	6 (32)	**OR 4.0 (1.0, 16.0)**
Gonzalez, 2015 [219, 229]	Buprenorphine + naloxone + memantine30 + CBT (group)	Buprenorphine + naloxone + memantine15 + CBT(group)	Abstinence (n, %)	3	28	23 (82)	27	9 (32)	**OR 9.2 (2.6, 32.3)**
	Buprenorphine + naloxone + memantine30 + CBT (group)	Buprenorphine + naloxone + placebo + CBT (group)	Abstinence (n, %)	3	28	23 (82)	32	10 (30)	**OR 9.2 (2.7, 31.5)**
	Buprenorphine + naloxone + memantine15 + CBT (group)	Buprenorphine + naloxone + placebo + CBT (group)	Abstinence (n, %)	3	27	9 (32)	32	10 (30)	OR 0.8 (0.3, 2.3)
	Buprenorphine + naloxone + memantine30 + CBT (group)	Buprenorphine + naloxone + memantine15 + CBT (group)	Opioid use (mean, SE)	3	27	0 (0)	24	0.27 (0.10)	Net Mean Diff. −0.3 (−23.9, 23.3)
	Buprenorphine + naloxone + memantine30 + CBT (group)	Buprenorphine + naloxone + placebo + CBT (group)	Opioid use (mean, SE)	3	27	0 (0)	29	0.39 (0.14)	Net Mean Diff. −0.39 (−40, 39.1)

Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI)
	Buprenorphine + naloxone + memantine15 + CBT (group)	Buprenorphine + naloxone + placebo + CBT (group)	Opioid use (mean, SE)	3	24	0.27 (0.10)	29	0.39 (0.14)	Net Mean Diff. −0.12 (−43.1, 42.9)
	Buprenorphine + naloxone + memantine30 + CBT (group)	Buprenorphine + naloxone + memantine15 + CBT (group)	Any adverse events (n, %)	3	27	11 (40.7)	24	7 (29.3)	OR 1.7 (0.5, 5.4)
	Buprenorphine + naloxone + memantine30 + CBT (group)	Buprenorphine + naloxone + placebo + CBT (group)	Any adverse events (n, %)	3	27	11 (40.1)	29	14 (48.3)	OR 0.7 (0.3, 2.1)
	Buprenorphine + naloxone + memantine15 + CBT (group)	Buprenorphine + naloxone + placebo + CBT (group)	Any adverse events (n, %)	3	24	7 (29.2)	29	14 (48.3)	0.4 (0.1, 1.4)
	Buprenorphine + naloxone + memantine30 + CBT (group)	Buprenorphine + naloxone + memantine15 + CBT (group)	Serious adverse events (n, %)	3	28	0 (0)	27	0 (0)	No events
	Buprenorphine + naloxone + memantine30 + CBT (group)	Buprenorphine + naloxone + placebo + CBT (group)	Serious adverse events (n, %)	3	28	0 (0)	32	0 (0)	No events
	Buprenorphine + naloxone + memantine15 + CBT (group)	Buprenorphine + naloxone + placebo + CBT (group)	Serious adverse events (n, %)	3	27	0 (0)	32	0 (0)	No events

Bold font indicates statistical significance.
Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; CM=contingency management; Educ = psychoeducation; group = at least one component of the intervention was delivered in a group format; MI = motivational interviewing; OR = odds ratio; SE = standard error

Alcohol Use Disorder

Seven comparative studies published between 2003 and 2016 assessed pharmaceutical interventions to reduce alcohol[230-239] use in 543 adolescents, total. Participants in the studies were on average 16 to 21 years of age (range across studies 13 to 21). Baseline and intervention details are given in Table 24.

Five of the seven studies were placebo-controlled evaluations of a single pharmaceutical agent (disulfiram, cyanamide or naltrexone). Two studies compared disulfiram to naltrexone. In addition to a medication, four of the seven studies included a behavioral intervention in both arms (e.g., education, MI, or CM).

Table 24. Baseline data and interventions: Pharmacologic treatments of alcohol use

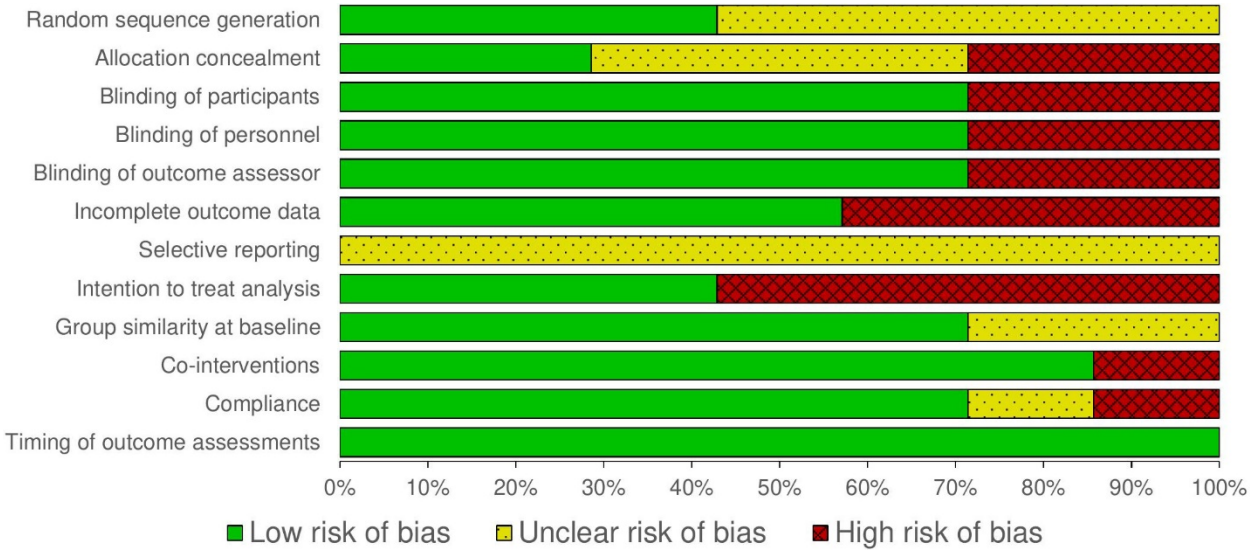
Author, Year	N	Substances Used	Severity	Ages [Eligible] Mean (SD)	Male %	Setting	Intervention Delivery	Arm Names
Miranda, 2014[232]	22	alcohol cannabis	PU	[15, 19] 18 (1.2)	36	outpatient research clinic	no detail (drug trial)	1. Placebo: "Placebo" 2. Naltrexone: "Naltrexone"
Niederhofer, 2003[233, 234]	26	alcohol	SUD	[16, 19] 17.1 (0.9)	38	hospital	no detail (drug trial)	1. Placebo: "Placebo" 2. Cyanamide: "Cyanamide"
Niederhofer, 2003[235]	49	alcohol	SUD	[16, 19] 16.9 (0.3)	69	hospital	no detail (drug trial)	1. Placebo: "Placebo" 2. Disulfiram: "Disulfiram"
Niederhofer, 2003[233, 234]	26	alcohol	SUD	[16, 19] nr	nr			1. Placebo: "Placebo" 2. Naltrexone: "Naltrexone"
O'Malley, 2015[236-239]	140	alcohol cannabis	PU	[18, 25] 21.5 (2.1)	69	outpatient research clinic	therapists and nurse practitioner (no detail)	1. Placebo+MI: "Placebo+MI" 2. Naltrexone+MI: "Naltrexone+MI"
De Sousa, 2008[230]	58	alcohol	SUD	[15, 18] 17.3 (nr)	nr	outpatient psychiatric center	no detail (drug trial)	1. Naltrexone+Educ (group): "Naltrexone" 2. Disulfiram+Educ (group): "Disulfiram"
De Sousa, 2014[231]	52	alcohol	SUD	[15, 18] 17.3 (nr)	nr	outpatient psychiatric center	no detail (drug trial)	1. Naltrexone+Educ (group): "Naltrexone" 2. Disulfiram+Educ (group): "Disulfiram"

Arm names = Intervention codes, (intervention modifiers) and [family subclassification]: "study arm name".

Abbreviations: Educ = psychoeducation; group = at least one component of the intervention was delivered in a group setting; MI = motivational interviewing; N=number randomized; nr = not reported; PU = problematic use; SD = standard deviation; SUD = substance use disorder

Risk of bias summaries are given in Figure 28. With the exception of de Sousa 2008,[230, 231] the studies were double blinded. Most studies did not conduct intention-to-treat analyses.

Figure 28. Pharmacologic Interventions for alcohol use: Percentage of studies in each risk of bias category



The reported outcomes included mean days of substance use, heavy use, abstinence, consequences, and adverse events. Results for each outcome are given in Table 25.

The six studies that reported on use outcomes in alcohol users reported that active interventions performed better than placebo for abstinence, use days, heavy drinking, or consequence scores in alcohol[230-233, 235, 236] or cannabis.[232, 240-244] Two studies compared naltrexone to placebo, and one study compared naltrexone and MI to placebo and MI. Niederhofer 2003 found naltrexone performed better than placebo for increasing days abstinent (mean difference 47.0, 95% CI 36.6 to 57.4) and abstinence overall (OR 4.00, 95% CI 1.37 to 11.7) at 3 months Similarly, Miranda 2014 found naltrexone performed better than placebo in reducing alcohol use days (mean difference −0.70, 95% CI −2.13 to 0.73) and heavy drinking days (mean difference −0.50, 95% CI −1.69 to 0.69) at 3 months, although the latter findings were not significant. When MI was combined with naltrexone and placebo, O'Malley 2015 observed similar results in favor of naltrexone for percent heavy drinking days, percent days abstinent, and alcohol consequences, however results were not significant (net mean difference −2.20, 95% CI −7.43 to 3.03; net mean difference 0.30, 95% CI −6.35 to 6.95; net mean difference −0.90, 95% CI−2.45 to 0.65, respectively) at 2 months Two studies by Niederhofer 2003 found disulfiram and cyanamide performed better than placebo for abstinence (disulfiram: OR 6.42, 95% CI 1.00 to 41.2; cyanamide: OR 6.42, 95% CI 1.00 to 41.2) and days abstinent (disulfiram: mean difference 38.8, 95% CI 16.0 to 61.7; cyanamide mean difference 43.8 95% CI 26.3 to 61.3) at 3 months. Finally, De Sousa 2008 found that disulfiram and education performed better than naltrexone and education for abstinence (OR 3.37, 95% CI 1.10 to 10.3).[230, 231] Across studies, adverse events were rarely reported, and where they were they were generally mild, including nausea, headache, and similar events. One study (O'Malley 2015) reported that there were no serious adverse events with either naltrexone or placebo; a second study (Miranda 2014) reported that there were two adverse events that lead to study discontinuation in the naltrexone arm (gastrointestinal symptoms) and none in the placebo arm.[232]

Table 25. Results: Pharmacologic treatments for alcohol use

Author, Year	Arm 1	Arm 2	Outcome	Time Point (Months)	Arm 1 N	Arm 1 Outcome	Arm 2 N	Arm 2 Outcome	Calculated Effect (95% CI)
O'Malley, 2015, [236-239]	Naltrexone + MI	Placebo + MI	Percent heavy drinking days	2	61	21.6 (16.1)	67	22.9 (13.2)	Net mean diff −2.20 (−7.43, 3.03)
			Percent of days abstinent per 8 weeks (mean, SD)	2	61	56.6 (22.5)	67	62.5 (15.8)	Net mean diff 0.30 (−6.35, 6.95)
			Alcohol consequences (BYAACS) (Mean, SD)	2	61	4.7 (3.6)	67	5.6 (3.9)	Net mean diff −0.90 (−2.45, 0.65)
			Serious adverse events n (%)	2	61	0 (0)	67	0 (0)	No events
Niederhofer, 2003 [235]	Disulfiram	Placebo	Abstinent from alcohol (n (%))	3	13	7 (54)	13	2 (15)	**OR 6.42 (1.00, 41.2)**
			Days Abstinent from alcohol per 3 months (Mean, SD)	3	13	68.5 (37.5)	13	29.7 (19.0)	**Diff 38.8 (16.0, 61.7)**
Niederhofer,2003 [233, 234]	Cyanamide	Placebo	Abstinent from alcohol (n, %)	3	13	7 (54)	13	2 (15)	**OR 6.42 (1.00, 41.2)**
			Days Abstinent from alcohol per 3 months (Mean, SD)	3	13	77.7 (24.3)	13	33.9 (21.0)	**Diff 43.8 (26.3, 61.3)**
Niederhofer, 2003, [233, 234]	Naltrexone	Placebo	Days Abstinent from alcohol per 3 months (Mean, SD)	3	30	69.8 (27.5)	30	22.8 (9.0)	**Diff 47.0 (36.6, 57.4)**
			Abstinence from alcohol (n, %)	3	30	20 (66.7)	30	10 (33.3)	**OR 4.00 (1.37, 11.7)**
Miranda, 2014, [232]	Naltrexone	Placebo	Alcohol use days, per 3 months (Mean, SD)	1	10	2.4 (1.4)	12	3.1 (2.0)	Diff −0.70 (−2.13, 0.73)
			Heavy drinking days (Mean, SD)	1	10	1.1 (1.0)	12	1.6 (1.8)	Diff −0.50 (−1.69, 0.69)
			Adverse events leading to withdrawal (n, %)	1	14	2 (14)	14	0 (0)	5.8 (0.25, 133.8)
De Sousa, 2008, [230]	Disulfiram + Educ (group)	Naltrexone + Educ (group)	Abstinent from alcohol (n, %)	6	29	23 (80)	29	15 (52)	**OR 3.6 (1.1, 11.4)**
De Sousa, 2014[231]	Disulfiram+ Educ (group):	Naltrexone+ Educ (group)	Abstinent from alcohol (n, %)	6	29	25 (86)	29	16 (54)	**OR 5.0 (1.4, 18.3)**

Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences.

Abbreviations: BYAACS = Brief Young Adult Alcohol Consequences Scale; CI = confidence interval; Educ = psychoeducation; group = at least one component of the intervention was delivered in a group setting; MI = motivational interviewing; OR = odds ratio; SD = standard deviation

Cannabis Use

We found two studies that enrolled 182 subjects (Table 26). Treatment with N-acetylcysteine did not result in over decreases in cannabis use days or cannabis abstinence. Risk of bias information is given in Figure 29. Treatment with topiramate+MI decreased cannabis use days, but not cannabis abstinence, compared to placebo+MI. However, treatment with Topiramate was associated with a higher odds of adverse events leading to withdrawal from treatment (Table 27).

Table 26. Baseline data and interventions: Pharmacologic treatments for cannabis

Author, Year	N	Substances Used	Severity	Ages [Eligible] Mean (SD)	Male %	Setting	Intervention Delivery	Arm Names
Gray, 2012[241-244]	116	cannabis	SUD	[13, 21] 18.9 (1.5)	72	outpatient research clinic	physician, physician assistant	1. Placebo+CM: "Placebo" 2. N-acetylcysteine+CM: "N- acetylcysteine"
Miranda, 2017[240, 245]	66	cannabis	PU	[15, 24] 18.8 (2.1)	46	outpatient research clinic	research staff (graduate students)	1. Topiramate+MI: "Topiramate" 2. Placebo+MI: "Placebo"

Arm names = Intervention codes, (intervention modifiers) and [family subclassification]: "study arm name".

Abbreviations: CM = contingency management; N=number randomized; PU = problematic use; SD = standard deviation; SUD = substance use disorder

Figure 29. Pharmacologic interventions for cannabis use disorder: Percentage of studies in each risk of bias category

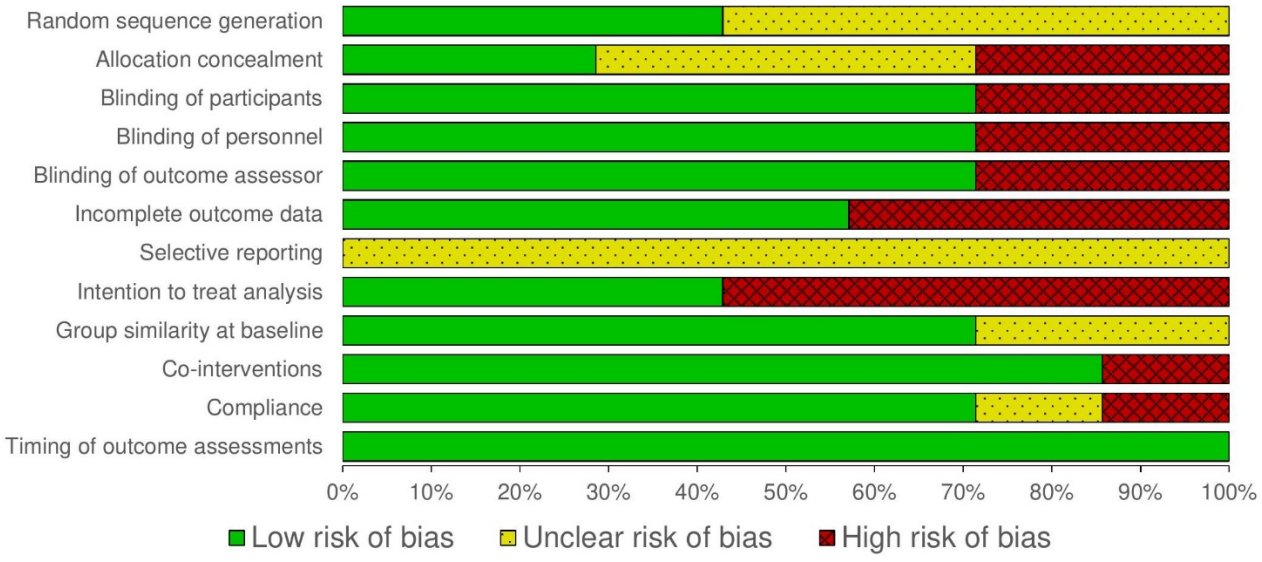


Table 27. Results: Pharmacologic treatments for cannabis use

Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time (mo)	Arm 1 N	Arm 1 Events (%)	Arm 2 N	Arm 2 Events (%)	Calculated Effect (95% CI)
Miranda, 2016, [240, 245]	Topiramate + MI	Placebo + MI	Abstinent from cannabis (n, %)	1	40	12 (30)	26	4 (16)	OR 2.4 (0.7, 8.3)
			Abstinent from cannabis (n, %)	1.5	40	8 (20)	26	4 (16)	OR 1.38 (0.4, 5.1)
			Cannabis use days (%, 95% CI)	1	40	53 (46, 59)	26	56 (48, 63)	Diff −3.0 (−12.1, 6.2)
			Cannabis use days (%, 95% CI)	1.5	40	41 (34, 47)	26	56 (47, 63)	**Diff −15.0 (−24.1, −5.9)**
			Serious adverse events n (%)	1	40	0 (0)	26	0 (0)	No events
			Adverse events leading to withdrawal n (%)	1	40	14 (35)	26	1 (4)	**OR 13.5 (1.6, 110)**
Gray, 2012, [241-244]	N-acetylcysteine + CM	Placebo + CM	Abstinent from cannabis (n, %)	2	58	11 (19)	58	6 (10.3)	OR 2.4 (0.8, 7.5)
			Cannabis use days (% decrease)	2	58	41.1 (4.3)	58	37.0 (4.4)	Diff −4.0 (−15.8, 7.9)
			Serious adverse events n (%)	2	58	0 (0)	58	0 (0)	No events

Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences.

Abbreviations: CI = confidence interval; CM = contingency management; group = at least one component of the intervention was delivered in a group setting; MI = motivational interviewing; OR = odds ratio

Comorbid Psychiatric Disorders in Adolescents With SUD

Key Points

- In studies of combined pharmacological and behavioral treatments for ADHD, bipolar disorder and depression for adolescents with SUD, the various interventions did not have consistent effects on the severity of the target psychiatric disorder.
- No study found significant increases or decreases in substance use outcomes. However, substance use outcomes were imprecisely estimated.

Specific Psychiatric Comorbidities

We found 10 RCTs that described treatments for specific psychiatric comorbidities in adolescents with a concurrent substance use disorder.[246-263] Studies were included if they reported the effects of pharmacologic treatment (with or without integrated behavioral interventions) on the severity of the comorbid mental health disorder and at least one substance use outcome. Given that substance use outcomes may depend on successful treatment of the psychiatric disorder, we have summarized both psychiatric and substance use outcomes.

Sample size per study ranged from 34 to 303 participants. The studies enrolled patients with one of four psychiatric diagnoses: Attention-deficit/hyperactivity disorder (ADHD; 3 studies

total; 1 with associated conduct disorder), depression (4 studies) and bipolar disorder (3 studies) who had concurrent substance use disorders for alcohol and/or cannabis, or other unspecified substances. Many adolescents in all studies used multiple substances, most commonly alcohol and cannabis and reported use of opioids, stimulants, sedatives, hallucinogens, and inhalants less commonly (<10% of participants).

Baseline and arm details are given in Table 28. Risk of bias summaries are given in Figure 30.

Table 28. Baseline data and interventions: Pharmacologic interventions for psychiatric comorbidities in adolescents with substance use disorders

Comorbidity	Author, Year	N	Substances Used	Severity	Ages [Eligible] Mean (SD)	Male %	Setting	Arm Names
ADHD	Riggs, 2011[252, 255, 257-259, 262, 263]	303	cannabis alcohol other drugs	SUD	[13, 18] 16.5 (1.3)	79	outpatient	1. Placebo+CBT+MI (integrated): "Placebo + CBT" 2. Methylphenidate+CBT+MI (integrated): "Osmotic-release methylphenidate + CBT"
ADHD	Thurstone, 2010[260]	70	cannabis alcohol other drugs	SUD	[13, 19] 16.1 (1.8)	79	outpatient (medications prepared by research pharmacist)	1. Placebo+CBT+MI (integrated): "Placebo + CBT/MI" 2. Atomoxetine+CBT+MI (integrated): "Atomoxetine + CBT/MI"
ADHD, conduct disorder	Riggs, 2004[264]	69	cannabis alcohol other drugs	SUD	[13, 19] 15.8 (1.4)	83	outpatient research clinic	1. Placebo (integrated): "Placebo" 2. Pemoline (integrated): "Pemoline"
bipolar disorder	Delbelo, 2017[253]	39	alcohol	SUD	[12, 25] 18 (3.1)	38	outpatient	1. Quetiapine+Topiramate (integrated): "Quetiapine+Topiramate" 2. Quetiapine+Placebo (integrated): "Quetiapine+Placebo"
bipolar disorder	Geller, 1998[251]	25	cannabis alcohol other drugs	SUD	[12, 18] 16.3 (1.2)	64	outpatient	1. Placebo (integrated): "Placebo" 2. Lithium (integrated): "Active"
bipolar disorder in a current manic or mixed episode	Delbelo, 2017[254]	75	cannabis	PU	[12, 18] 17.4 (0.2)	49		1. Quetiapine+Topiramate (integrated): "Quetiapine+topiramate" 2. Quetiapine+Placebo (integrated): "Quetiapine+placebo"
depression	Cornelius, 2009[247]	50	alcohol	SUD	[15, 20] nr	44	outpatient research clinic	1. Placebo+CBT+MI (integrated): "Placebo" 2. Fluoxetine+CBT+MI (integrated): "Fluoxetine"

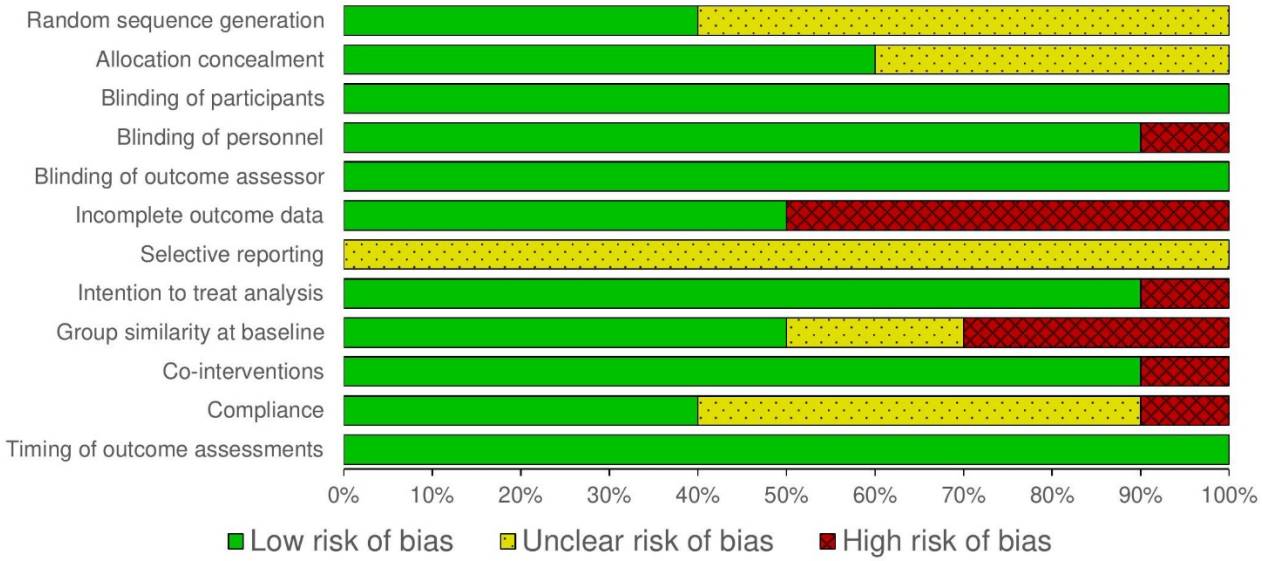
Comorbidity	Author, Year	N	Substances Used	Severity	Ages [Eligible] Mean (SD)	Male %	Setting	Arm Names
depression	Cornelius, 2010[246, 249, 265]	70	cannabis alcohol	SUD	[14, 25] 21.1 (2.4)	61	outpatient research clinic	1. Placebo+CBT+MI (integrated): "Placebo" 2. Fluoxetine+CBT+MI (integrated): "Fluoxetine"
depression	Findling, 2009[250]	34	cannabis alcohol	SUD	[12, 17] 16.5 (1.1)	85	outpatient research clinic	1. Placebo (integrated): "Placebo" 2. Fluoxetine (integrated): "Fluoxetine"
depression	Riggs, 2007[256, 261]	126	cannabis alcohol other drugs	SUD	[13, 19] 17.2 (1.7)	67	outpatient research clinic	1. Placebo+CBT: "Placebo + CBT" 2. Fluoxetine+CBT: "Fluoxetine + CBT"

Arm names = Intervention codes, (intervention modifiers) and [family subclassification]: "study arm name".

Abbreviations: ADHD = attention-deficit/hyperactivity disorder; CBT = cognitive behavioral therapy; integrated = intervention as a whole was designed to treat substance use disorder/problematic use and at least one other diagnosis (e.g., mental health); MI = motivational interviewing; N=number randomized; nr = not reported; PU = problematic use; SD = standard deviation; SUD = substance use disorder

The most commonly observed risk of bias concerns related to incomplete outcome data, group similarity at baseline and compliance (Figure 30).

Figure 30. Pharmacologic interventions for psychiatric comorbidities in adolescents with substance use disorders: Percentage of studies in each risk of bias category



The reported outcomes included severity of comorbidity condition, mean days of substance use, heavy use, abstinence, consequences, and adverse events. Full results for each outcome in studies treated for co-existing ADHD, depression, and bipolar disorder are given in Tables 29, 30, and 31, respectively.

The three studies that reported on outcomes in not otherwise specified substance abuse populations with comorbid ADHD found no impact of pharmacologic agents pemoline, atomoxetine, or fluoxetine (with or without behavioral interventions) on ADHD symptoms, use days, or adverse events.

Four studies that reported on outcomes in populations defined by alcohol, cannabis, or not otherwise specified substance abuse populations with comorbid depression. Three studies found no impact of fluoxetine (with or without CBT + MI) on symptoms of depression, use days, problem scores (e.g., abuse symptoms and dependence symptoms). The exception is Riggs et al., 2007.[256] This study enrolled patients with substance use and depression and compared fluoxetine + MI+CBT, with placebo+MI+CBT. They found a net mean difference of −4.2 (95% CI −9.7, −2.0) suggesting an improvement in depression symptoms as measured by the Children's Depression Rate Scale, Revised (CDRS-R).

The three studies that reported outcomes in populations defined by alcohol and cannabis use with comorbid bipolar disorder found no impact of lithium or quetiapine + topiramate on symptoms of mental health and of adverse events observed, most either occurred rarely, or where presented, were comparable between groups.

Table 29. Results: Pharmacologic interventions for ADHD in adolescents with substance use disorders

Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time (mo)	Arm 1 N	Arm-1 Outcome	Arm-2 N	Arm-2 Outcome	Effect (95% CI)
Riggs, 2004 [264]	Pemoline	Placebo	CHIS	4	34	−12.2 (−18.5, −5.9)	34	−7.2 (−12.0, −2.4)	MD −5.0 (−12.9, 2.9)
Riggs, 2011 [252, 255, 257-259, 262, 263]	Methylphenidate + CBT + MI	Placebo + CBT + MI	ADHD-RS	4	151	−19.2 (−21.2, −17.2)	152	−21.2 (−23.2 −19.2)	MD 2.0 (−0.9, 4.9)
			Uses days (past 28 days non-tobacco)	4	151	−5.7 (−7.2, −4.1)	152	−5.2 (−6.8, −3.6)	MD−0.5 (−2.7, 1.7)
Thurstone, 2010 [260]	Ato + CBT + MI + Fam	Placebo + CBT + MI + Fam	ADE - Vomiting (%)	3	32	16	33	7	***OR 3.7 (1.3, 11.0)***
			ADE - Drowsiness (%)	3	32	16	33	14	OR 1.4 (0.51, 3.6)
			ADE – Dif staying asleep (%)	3	32	16	33	20	OR 0.6 (0.4, 1.7)
			ADE – Abdominal Pain (%)	3	32	18	33	15	OR 1.5 (0.6, 4.1)
			ADE – Nasal Congestion (%)	3	32	19	33	17	OR 1.4 (0.5, 3.7)
			ADE – Difficulty falling asleep (%)	3	32	19	33	23	OR 0.6 (0.2, 1.8)
			ADE – Appetite decrease (%)	3	32	19	33	12	OR 2.6 (0.4, 7.0)

Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time (mo)	Arm 1 N	Arm-1 Outcome	Arm-2 N	Arm-2 Outcome	Effect (95% CI)
			ADE – Difficulty concentrating (%)	3	32	21	33	15	OR 2.3 (0.4, 6.2)

Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences.

Abbreviations: ADE = adverse event; ADHD-RS = Attention-Deficit/Hyperactivity Disorder Rating Scale; Ato = Atomoxetine; CBT = cognitive behavioral therapy; CHIS = Conners Hyperactivity-Impulsivity scale (parent related); CI = confidence interval; Fam = family based therapy; MD = mean difference; MI = motivational interviewing; N = number of participants analyzed; OR = odds ratio

Table 30. Results: Pharmacologic interventions for depression in adolescents with substance use disorders

Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time (mo)	Arm 1 N	Arm 1 Outcome	Arm 2 N	Arm 2 Outcome	Effect (95% CI)
Cornelius 2009 [247]	Fluoxetine + CBT + MI	Placebo + CBT + MI	Depression (BDI)	3	24	MD −10.46 (−13.8, −7.1)	26	MD −11.7 (−15.3, −8.0)	NMD 1.2 (−3.8, 6.2)
			Problems (alcohol sxs)	3	24	MD −2.66 (−3.5, −1.8)	26	MD −2.5 (−3.6,−1.5)	NMD −0.1 (−1.5,1.2)
Cornelius, 2010 [246, 249, 265]	Fluoxetine + CBT + MI	Placebo + CBT + MI	Use days (heavy drinking days/wk)	3	34	MD −0.03 (−0.3, 0.3)	36	MD −0.12 (−0.4, 0.2)	NMD 0.09 (−0.4,0.5)
			Problems (alcohol abuse sxs)	3	34	MD −0.1 (−0.3, 0.1)	36	MD −0.19 (−0.4, 0.01)	NMD 0.11 (−0.2, 0.4
			Problems (dep sxs)	3		MD −0.6 (−1.1, −0.1)		MD −0.25 (−0.7, 0.2)	NMD −0.3 (−1.0, 0.3)
			Use days (per week)	3	34	MD −0.7 (−1.54, 0.08)	36	MD −1.2 (−1.9,−0.6)	NMD 0.5 (−0.6, 1.6)
			Problems (abuse sxs)	3	34	MD −0.8 (−1.1, −0.4)	36	MD −0.7 (−1.0, −0.5)	NMD −0.04 (−0.4,0.4)
			Problems (dep sxs)	3	34	MD −1.59 (−2.2, −1.0)	36	MD −2.0 (−2.6,−1.5)	NMD 0.5 (−0.4, 1.3)
Riggs 2007 [256, 261]	Fluoxetine + CBT + MI	Placebo + CBT + MI	Depression CDRS-R	4	63	MD −24.8 (−27.5, −22.0)	63	MD −18.9 (−21.6, −16.2)	***NMD −5.9 (−9.7, −2.0)***
			AOD use days (per month)	4	63	MD −3.94 (−6.8, −1.1)	63	MD −4.7 (−7.6, −1.8)	NMD 0.8 (−3.3, 4.8)
Findling 2009 [250]	Fluoxetine	Placebo	Depression CDRS-R	2	18	MD −18.4 (−19.7, −17.1)	16	MD −22.6 (−24.1, −21.1)	***NMD 4.2 (2.2, 6.2)***
			AOD abstinence	2	12	8	13	10	OR 0.6 (0.1, 3.5)

Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences.

Abbreviations: AOD = alcohol and other drugs; BDI = Beck Depression Inventory; CBT = cognitive behavioral therapy; CDRS-R = Children's Depression Rating Scale-Revised; CI = confidence interval; dep = dependence; MD = mean difference; MI = motivational interviewing; N = number of participants analyzed; NMD = net mean difference; OR = odds ratio; sxs = symptoms

Table 31. Results: Pharmacologic interventions for bipolar disorder in adolescents with substance use disorders

Study Author, Year, PMID	Arm 1	Arm 2	Outcome	Time (mo)	Arm 1 N	Arm 1 No. events	Arm 2 N	Arm 2 No. Events	OR (95% CI)
Geller, 1998 [251]	Lithium	Placebo	CGAS >=65 (%)	1.5	13	6	12	1	9.4 (0.9, 95.9)
Delbelo 2017 [253]	Quetiapine/Topiramate	Quetiapine + Placebo	ADE – Suicidal Ideation (N)	4	18	2	21	8	0.2 (0.04, 1.1)
			ADE – Suicidal attempt (N)	4	18	0	21	1	0.6 (0.02, 18.1)
			ADE – Sedation (N)	4	18	11	21	4	**6.7 (1.6, 28.3)**
			ADE – Dif Arousing (N)	4	18	9	21	3	**6.0 (1.3, 27.8)**
Delbelo 2017 [254]	Quetiapine/Topiramate	Quetiapine + placebo	ADE- Dry mouth (N)	4	38	23	37	30	0.4 (0.1, 1.0)
			ADE- Excitement (N)	4	38	5	37	0	11.1 (0.6, 210.3)
			ADE-Dif Staying Asleep (N)	4	38	12	37	20	0.4 (0.2, 1.0)
			ADE-Dif Falling Asleep (N)	4	38	12	37	20	0.4 (0.15, 1.0)
			ADE- Pregnancy (N)	4	38	0	37	1	0.5 (0.02, 14.8)
			ADE- Suicidal Ideation (N)	4	38	1	37	0	2.0 (0.06, 60.6)
			ADE- Hospitalization (N)	4	38	4	37	5	0.8 (0.2, 3.1)
			ADE- Any (N)	4	38	23	37	30	0.4 (0.1, 1.0)

Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for difference.

Abbreviations: ADE = adverse event; CGAS = Children's Global Assessment Scale; CI = confidence interval; N = number of participants analyzed; OR = odds ratio

Discussion

Key Findings

Most studies of brief behavioral interventions evaluated motivational interviewing (MI) compared to treatment as usual (TAU). These studies enrolled adolescents who often had problematic use of both alcohol and cannabis. Some heterogeneity in effects between studies was found, but MI resulted in overall decreases in heavy alcohol use days (i.e., binge drinking), overall alcohol use days and may reduce all substance use related problems compared to TAU. However, brief MI does not reduce days of cannabis use compared to TAU.

Longer term (i.e., "nonbrief") behavioral interventions were diverse and often combined multiple intervention components. This diversity severely limited our ability to evaluate their efficacy compared to TAU and to each other. Nevertheless, our analyses did suggest that family-based therapies (Fam) may most effectively decrease alcohol use days, and may be more effective than ICM, CBT and MI in reducing days of alcohol use. We found no evidence of efficacy for any intervention in decreasing days of cannabis use. Indeed, summary estimates suggest that some interventions (CBT, CBT+MI, CBT+MI+CM and Educ) increase cannabis use relative to TAU.

Both MI and CBT reduce days of alcohol and other drug use relative to TAU, with MI more effective than PeerGroup, CBT+MI, Fam, CBT+ICM, CBT+MI+ICM, CBT and ICM. Illicit drug use decreased for CBT+MI compared to TAU.

Overall, our findings suggest that that effects may vary by substance for both brief and nonbrief interventions. However, these conclusions are based on separate analyses (of overlapping groups of studies) that are not directly comparable.

Existing systematic reviews of the general population of college students who drink alcohol found that, on average, compared to no intervention, behavioral interventions resulted in reduced alcohol use for up to about 6 months, but these effects waned in the long term. However, behavioral interventions resulted in fewer alcohol-related problems over the medium to long term. One SR found that, by indirect comparison, face-to-face interventions provide larger and more enduring effects than computer-delivered interventions. Two SRs focused on college students who engaged in heavy or hazardous alcohol use. Brief, single-session interventions and the commercially available BASICS program were found to reduce alcohol use compared with no intervention. Among the brief behavioral interventions, MET/MI had the strongest effect. Two SRs focused on college students mandated to attend alcohol programs. On average, alcohol use decreased in the short- to medium-term regardless of intervention, but mostly did not persist. Four specific commercially available interventions were found to be more effective in the short term than others.

For opioid use disorder, longer courses (2 to 3 months) of buprenorphine are more effective than shorter courses (14 to 28 days) to reduce opioid use and achieve abstinence.

For alcohol and cannabis use disorder, evidence is insufficient regarding the effects of medications adding medications to treat substance use disorders. There is insufficient evidence relating to the effects of pharmacologic treatments used for the treatment of psychiatric comorbidities, depression, ADHD, and bipolar disorder in patients with concomitant substance use disorders.

When assigning strength of evidence (SoE) we considered various concepts including whether the conclusions are based on direct (head-to-head) or indirect comparisons (for which there were no head-to-head comparisons) and whether the reported outcomes are direct (true) measures of

the outcome of interest. In the network meta-analyses we conducted related to nonbrief behavioral interventions, conclusions are based predominately on indirect evidence, with sparse direct evidence. Although there was some variability in the definitions of use days, abstinence and drug related problems, these were deemed to be sufficiently minor so as not to affect the overall directness. In contrast, for subpopulations and additional outcomes that were not meta-analyzed, conclusions were downgraded for being indirect if the outcomes were generally not well-defined and likely varied across studies.

The strength of evidence (SoE) for each conclusion, presented in Table 32, is based on a qualitative combination of the summary risk of bias across all relevant studies, the consistency of the studies, the precision of the available estimates, and the directness of the evidence.

Table 32. Evidence profile for interventions for substance use disorders and problematic use in adolescents

Inter-ventions	Topic	Outcome	Comparison	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Overall SoE	Conclusion statements
Brief Behavioral Inter-ventions	***Alcohol outcomes***	Heavy use days	MI vs. TAU	7 (1248)	Moderate	Consistent	Imprecise	Direct	**Low**	**MI more effective than TAU**
		Use days	MI vs. TAU	10 (2153)	Moderate	Consistent	Precise	Direct & Indirect	**Moderate**	**MI more effective than TAU**
		Abstinence	MI vs. TAU	7 (2482)	Moderate	Consistent	Imprecise	Direct & Indirect	Insufficient	None
	Cannabis outcomes	Use days	MI vs. TAU	13 (2386)	Moderate	Consistent	Precise	Direct & Indirect	**Moderate**	**MI *not* more effective than TAU**
		Abstinence	MI vs. TAU	6 (1119)	Moderate	Consistent	Imprecise	Direct	Insufficient	None
	Substance related problem scores	Multiple substance use problem scales	MI vs. TAU	9 (1854)	Moderate	Consistent	Imprecise	Direct & indirect	**Low**	**MI more effective than TAU**
			MI vs. Educ	3 (646)	Moderate	Inconsistent	Imprecise	Direct	Insufficient	None
Nonbrief Behavioral Inter-ventions	***Alcohol outcomes***	Use days	Network of 11 interventions	11 (2005)	Moderate	Unclear	Precise	Direct (sparse) & indirect	**Low**	**Fam more effective than TAU, ICM, CBT, MI**
	Cannabis outcomes	Use days	Network of 13 Interventions	11 (1643)	Moderate	Unclear	Imprecise	Direct (sparse) & Indirect	**Low**	**CBT, CBT+MI, CBT+MI+ CM, Educ *less* effective than TAU**
	Alcohol and other drug use	Use days	Network of 8 interventions	9 (1170)	Moderate	Unclear	Precise	Direct (sparse) & indirect	**Low**	**MI, CBT more effective than TAU**

Inter-ventions	Topic	Outcome	Comparison	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Overall SoE	Conclusion statements
Nonbrief Behavioral Inter-ventions (contin-ued)	***Illicit drug use***	Use days	Network of 7 interventions	5 (1310)	Moderate	Unclear	Precise	Direct (sparse) & indirect	**Low**	**CBT+MI more effective than TAU**
		Use days			Moderate	Unclear	Imprecise	Direct (sparse) & indirect	Insufficient	None (for comparative effects)
	Opioid use: Medications, plus behavioral therapies	*Use: abstinence or reported use*	BUP (longer vs. shorter treatment duration)	2 (207)	Moderate	Consistent	Imprecise	Direct	**Low**	**Longer duration buprenor-phine more effective**
			BUP vs. Clonidine	1 (36)	Low	NA	Imprecise	Direct	Insufficient	None
			BUP (± 2 doses of MEM	1 (80)	Low	NA	Imprecise	Direct	Insufficient	None
	Alcohol use: Medications	*Use: abstinence and/or reported use*	Cyanamide vs. Placebo	1 (26)	Low	NA	Imprecise	Direct	Insufficient	None
			Disulfiram vs. placebo	1 (110)	Low	NA	Imprecise	Direct	Insufficient	None
			Naltrexone vs. Placebo†	3 (188)	Low	Inconsistent (effective in 1 of 3 studies)	Imprecise	Direct	Insufficient	None
			Disulfiram+ Educ(group) vs. Naltrexone+ Educ(group)	2 (110)	Moderate	Consistent (single center)	Imprecise	Direct	Insufficient	None
	Cannabis use: Medications		NAC+CM vs. Placebo+CM	1 (116)		NA	Imprecise	Direct	Insufficient	None
			TOP+MI vs. Placebo+MI	1 (66)		Inconsistent	Imprecise	Direct	Insufficient	None

Abbreviations: BUP = Buprenorphine/Buprenorphine-naloxone; CBT = cognitive behavioral therapy; CM = contingency management; Educ = psychoeducation; Fam = family therapy; ICM = intensive case management; MEM = Memantine; MI = motivational interviewing; NAC = N-acetylcysteine; SoE = strength of evidence; TAU = treatment as usual; TOP = Topiramate

†One study compared Naltrexone+MI with Placebo+MI.

Findings in Relationship to What Is Already Known

Brief Behavioral Interventions

Our review of randomized controlled trials (RCTs) found that brief MI or motivation enhancement therapy (MET) reduces heavy alcohol use and overall alcohol use compared to TAU in adolescents with problematic alcohol use. Across brief behavioral interventions, we concluded that MI is more effective than TAU in reducing substance use associated problems. These findings are generally consistent with the recent systematic review with meta-analysis (SR/MA) of experimental and quasiexperimental studies by Tanner-Smith and Lipsey.[266] Combining across multiple related outcomes and different interventions using a standardized effect size metric, they conclude that adolescents ages 11 to 18 who received brief alcohol interventions had lower levels of self-reported alcohol consumption and alcohol-related problems, and concluded that MI/MET strategies were most effective.[266] In a subsequent paper, Tanner-Smith and Risser explore the variability of effects across different outcome measures.[267]

We found that MI does not reduce days of cannabis use compared to TAU. Recent reviews have reached mixed conclusions regarding effects on cannabis use. A SR/MA by Li et al. that identified 10 randomized trials evaluating MI interventions for illicit drug use in adolescents.[268] They pooled use of multiple illicit substances, including cannabis (80%), cocaine (30%) and amphetamines/MDMA (20%) and concluded that there was no statistically significant effect of MI on drug use behaviors.[268] A SR/MA of adolescents and young adults,[269] found that brief behavioral interventions targeting both alcohol and other illicit drugs effectively reduced use of "both of these substances." The review concludes that brief interventions that targeted only alcohol had no statistically significant secondary effects on untargeted illicit drug use.[269] Our analyses of cannabis outcomes included all studies that reported a cannabis-specific outcome. As we discuss in the *Limitations of the Evidence Base* section, it was often unclear if specific substance use was targeted, and study participants often used multiple substances.

Given the apparent heterogeneity of treatment effects for alcohol and cannabis, it may be problematic to interpret effects for outcomes that combine multiple substances (e.g., alcohol, cannabis, and other drugs), as prior SRs have done.

Nonbrief Behavioral Interventions

Previous SRs have highlighted specific interventions and combinations of interventions as well established or showing particular promise for reducing substance use in adolescents. A 2018 SR and qualitative synthesis by Hogue et. al. identified several interventions as "well established."[27] cognitive behavioral therapy (CBT, delivered both individually and in group format), Fam (delivered with an ecological orientation), MI + CBT, and MI + CBT + Fam (delivered with a behavioral orientation). Additional models were identified as "probably efficacious," including: MI, Fam (delivered with a behavioral orientation), and several multi-component interventions the include contingency management.[27]

The SR/MA by Tanner-Smith et. al. of 61 experimental or quasi-experimental studies concluded that "most substance use treatment programs were beneficial in helping adolescents reduce their substance use when those treatment programs provide tailored treatment services beyond standard community services. Fam and CBT programs showed particular promise of effectiveness, and no program types showed evidence of harmful effects."[270]

We performed separate network meta-analyses (NMA) for each substance specific outcome. This results in sparse networks and a reliance on primarily indirect evidence. Our NMA of the alcohol use days outcome suggests that intensive behavioral intervention with the entire family present (Fam) may be particularly effective. Furthermore, Fam may be more effective than intensive case management, CBT and MI.

We found little evidence to support the effectiveness of any intervention to reduce cannabis use days. Indeed, we found that CBT, CBT+MI and CBT+MI+CM and Educ may result in relative **increases** in cannabis use compared to TAU. These conclusions are tentative, but if true, imply that there may be treatment effect heterogeneity by substance.

Pharmacologic Interventions

Only four studies evaluated treatment of opioid use disorder in adolescents or young adults. All addressed pharmacologic options for short-term opioid detoxification. There are currently three Food and Drug Administration (FDA)-approved medications for opioid use disorder in adults. For two of these (naltrexone and methadone) we found no studies in adolescents. None of the included studies evaluated long-term medication-assisted treatment.

Pharmacologic Treatment of Psychiatric Comorbidities in Adolescents With Substance Use Disorders

The narrative review by Brewer et. al. concludes that psychiatric and substance use disorder comorbidity is the rule rather than the exception.[271] We reviewed outcomes from 10 RCTs of pharmacotherapies used for ADHD, bipolar disorder and depression in adolescents with concomitant substance use. No study demonstrated superior comparative effects on substance use outcomes in subjects given pharmacotherapy compared to placebo. However, most studies were small, with resultant imprecision (wide confidence intervals). Of note, a single RCT[256, 261] that evaluated fluoxetine with CBT+MI for comorbid depression found improvements in depression. Notably, none of the other 9 RCTs found demonstrated an improvement in the target psychiatric disorder.

Applicability

A number of factors may limit the applicability of our findings.

We aggregated brief behavioral interventions from studies done in various settings (e.g., emergency department (ED), inpatient, outpatient primary care, juvenile justice). Treatment effects may be moderated by context specific factors. For example, brief interventions in the ED after an alcohol-related presentation may represent a "teachable moment," or alternatively, the saliency of the event may prompt self-change.[272]

The diagnostic criteria for substance use disorders are well defined, albeit with variation by DSM version. However, our pragmatic inclusion criteria for problematic use necessarily defined a more heterogeneous group of substance users, likely with substantial variability in the degree of impairment.

Study inclusion criteria varied with regards to the primary substance of misuse, as detailed in Appendix D Some studies explicitly focused on adolescents who primarily misused a specific substance (i.e. alcohol or cannabis) and reported use-related outcomes for that substance only. However, other studies enrolled adolescents who misused a combination of substances, most commonly alcohol and cannabis, and reported some combination of cannabis and alcohol

outcomes. Other studies reported outcomes for composite use of unspecified substances (e.g., "illicit drug use").

Despite this apparent heterogeneity of inclusion criteria, most studies enrolled alcohol and cannabis users (see Appendix Tables D-1 and D-2), with a minority using other drugs. Within studies, details of specific substances use were often incompletely reported (see Appendix Table D-3).

Behavioral interventions sometimes explicitly targeted multiple substances, e.g. alcohol and other drug use. Unlike some pharmacologic interventions, behavioral interventions are not inherently substance-specific. We therefore chose to aggregate our analysis by substance specific use outcomes, rather than attempting to disentangle effects for a specific use disorder or problematic use of alcohol or cannabis. This choice may limit the applicability of our conclusions to users of a single substance. Furthermore, this approach does not account for possible interaction effects between outcomes within a study, e.g. interventions that successfully target alcohol use might result an increase cannabis use due to substitution of cannabis for alcohol.[273]

The specific outcomes reported in each substance-of-use category are detailed for each study in Appendix E-1 (Brief interventions) and E-2 (Nonbrief interventions). Table 33 below, summarizes the number of behavioral studies in each intervention category that reported an alcohol outcome only, a cannabis outcome only, or both an alcohol and a cannabis outcome.

Table 33. Number of meta-analyzed studies reporting outcomes for alcohol only, cannabis only, or both

Intervention Type	AlcoholOnly Outcomes	Cannabis-Only Outcomes	Alcohol & Cannabis
Brief	7	7	7
Intensive	6	10	9

Alcohol only outcomes: heavy-use days, use days, abstinence; Cannabis-only outcomes: use days, abstinence

A few studies explicitly focused on adolescents with SUD and a specific comorbid mental health diagnosis, whereas most studies focused on adolescents with SUD and often did not report on the frequency of comorbid psychiatric comorbidities.

Thus, even when samples were selected based on a specific substance or specific comorbid diagnosis, the populations identified were generally heterogeneous samples of polysubstance using adolescents, many of whom likely have psychiatric comorbidities.

Interventions identified across studies are multicomponent, complex interventions. Rather than simply comparing "brand name" therapy models, we attempted to identify a common set of core intervention components. Classification of active intervention components was dependent on the quality of reporting, and in many cases, specific intervention components were not well described. Determination of the list of classification components of interest and classification of the components for each study required judgements.

Comparator conditions – often generally described as treatment as usual (TAU) – were particularly challenging to classify, as the TAU category defines a heterogeneous collection of often poorly described active interventions. Any classification of interventions cannot perfectly

capture the complexity of these interventions and relies on highly variable reporting in published reports.

Implications for Clinical and Policy Decision Making

As summarized in Table 32, there is evidence for the effectiveness of brief behavioral interventions for adolescents with problematic alcohol use. This supports the expansion of current initiatives to implement screening, brief intervention and referral to treatment (SBIRT) adolescents with alcohol use.[274] However, based on the evidence, it should not be assumed that brief interventions have equal effects on alcohol and cannabis. In particular, brief motivational interviewing appears to be ineffective for adolescents with problematic cannabis use.

Limited evidence suggests that family focused behavioral interventions may be particularly effective in the treatment of alcohol use disorder. No intervention or combination of intensive interventions demonstrated a definite positive effect on increasing abstinence or decreasing overall cannabis use.

Evidence that longer courses of buprenorphine are more effective in the short-term management of opioid withdrawal supports recommendations for increased utilization of buprenorphine for longer-term maintenance therapy.[17, 275]

Limitations of the Systematic Review Process

In our analyses, we used both direct and indirect information to inform comparisons between interventions. When interpreting the results, it is important to note that indirect comparisons rely on an assumption of consistency between indirect and direct evidence. For nonbrief behavioral interventions, the multiplicity of interventions and intervention components resulted in very sparse direct evidence.

We chose to rate an intervention component as present only if the intervention was well-specified, as evidenced by use of a manual or fidelity monitoring. There were some multi-component interventions in which the intervention was well-specified and monitored, but specific elements were much less so. Decisions about how to code these interventions were challenging and were directly influenced by the quality of intervention reporting. The use of a codebook and independent coding by three raters, one of which was a content expert and one of which was a methodological expert in multi-component interventions, helped to ensure that we used a consistent approach.

Limitations of the Evidence Base

For many topics, evidence was sparse and indeterminate — or absent entirely. The bulk of evidence relates to adolescents with problematic use or substance use disorders related to alcohol or cannabis.

Overall, we found very few studies in adolescents or young adults (ages 25 or less) that evaluated pharmacologic or combined pharmacologic and behavioral interventions. We identified 988 trials in adults that enrolled participants 18 years and older but found none that provided an extractable analysis of the adolescent/young adult subgroup.

The evidence regarding treatment of psychiatric comorbidities is quite limited. For the treatment of ADHD, we found no studies that evaluate agents that may have less potential for abuse (e.g., guanfacine and clonidine).

Outcomes were measured and reported inconsistently. Most studies reported multiple outcomes. The most commonly reported outcome across studies was self-reported substance use days. However, use days were summarized over variable denominators (e.g., 7, 30, or 90 days), expressed as percent or log- or square root-transformed. Other studies quantified indicators of abstinence or substance-related problems use using a variety of scales. The lack of consistently reported outcomes across studies reduced the number of available comparisons.

The available evidence was too sparse to allow identification of key ingredients of successful interventions (moderators of treatment effect) or how intervention effects differ across demographic groups.

Studies took a wide variety of approaches to missing data in subjects who dropped out of treatment. When available, we preferred intention-to-treat analyses or model-based expected means. However, studies often reported only raw summary data based on number analyzed.

Recommendations for Future Research

There is a need to adopt a set of core outcome measures and standard approaches to reporting of these outcomes. For example, among studies to date, a wide range of outcomes have been used, including measures of frequency of use, abstinence, and substance-related problems. Even among studies that measure "frequency of use," the metrics used (e.g., count of days, proportion of days), specific substances of focus, and recall periods vary substantially. This required us to synthesize data over different recall periods. If all studies had consistently reported a core outcome set utilizing common measures, our summary findings would have been more reliable. Ideally, abstinence and use in studies would be modeled jointly, and may best be synthesized using a hurdle model utilizing individual patient data from individual studies.[276, 277]

The observed variability of treatment effects by substance suggests it may difficult to interpret composite outcomes (i.e., *alcohol and other drugs*, *illicit drugs* and *other drugs*). If treatment effects vary by substance, estimates of composite effects will be determined by the relative proportion of alcohol, cannabis, and other drug use in individual studies. Furthermore, the increasing potency of cannabinoid products over time may impact response to therapy.[278]

A core outcome set would be especially valuable if it included standardized definitions of patient-centered outcomes, such as adolescent functioning in school, peer, and family domains. Some studies included secondary functional outcomes, but such outcomes were included inconsistently and varied across reports. More data on functional outcomes are needed to determine whether the reductions in days of use documented in this report translate into meaningful clinically improvements for adolescents.

To support evidence synthesis, studies need to more clearly describe intervention components received by study participants, including those assigned to TAU. For example, rather than simply stating that an intervention was designed to "build motivation" or "build skills," investigators should clearly explicate the underlying theoretical orientation of the intervention. In addition, each unique aspect of a multi-component intervention should be well-described, with references to a manual and supportive source materials. Data on fidelity monitoring should ideally be provided for each major component underlying the intervention.

Large "adult" trials that enroll older adolescents (age 18 to 20) should consider reporting this subgroup.

Future research should also seek to clarify whether specific subpopulations may benefit from specific intervention components. Specifically, studies should seek to clarify which interventions are most effective for a given primary substance of misuse, severity of use, and how

effectiveness is moderated by the presence of co-occurring psychiatric disorders. Much of this research in the United States is funded by the National Institutes of Health via the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Harmonized guidance from these agencies with respect to core outcomes might be particularly impactful.

Conclusions

Compared with TAU (e.g., brief advice and a handout), brief MI for adolescents with problematic substance use increases the likelihood of abstinence from alcohol and reduces both heavy alcohol use and overall days of use. However, brief MI did not decrease cannabis use. MI may decrease problems related to substance use, such as missed school or work or getting into trouble.

Among intensive interventions, Fam (with a focus on intervening in the entire family system) may be the most effective in reducing both days of heavy alcohol and overall alcohol use.

For opioid use disorder, buprenorphine and buprenorphine-naloxone are more effective in the short term management of opioid withdrawal if they are tapered over a longer period of time (i.e. 12 weeks versus 2 weeks, 56 days versus 28 days). Studies of long-term pharmacologic and/or behavioral treatment of opioid use disorder are urgently needed.

Further research is needed to identify: 1) brief and more intensive interventions for problematic cannabis use and cannabis use disorder, 2) effective combinations of behavioral treatments and medication to treat alcohol and cannabis use disorders, and 3) interventions that improve outcomes that are most meaningful to adolescents, such as better functioning in school and improved relationships with peers and parents.

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Abbreviations and Acronyms

AACAP	American Academy of Child and Adolescent Psychiatrists
AAP	American Academy of Pediatrics
ACC	Assertive continuing care
ACRA	Adolescent community reinforcement approach
ADE	adverse event
ADHD	attention deficit hyperactivity disorder
ADHD-RS	Attention Deficit Hyperactivity Disorder Rating Scale
ADI	Adolescent Diagnostic Interview
Ato	atomoxetine
AUD	alcohol use disorder
AUDIT	Alcohol Use Disorders Identification Test
BAC	blood alcohol concentration
BASICS	Brief Alcohol Screening and Intervention for College Students
BDI	Beck's depression inventory
CDRS-R	Children's Depression Rating Scale, Revised
BSFT	Brief strategic family therapy
CBT	cognitive behavioral therapy
CGAS	Children's Global Assessment Scale
CI	confidence interval
CM	contingency management
CRAFT	Community Restitution Apprentice-Focused Training
CrI	credible interval
DSM-III	Diagnostic and Statistical Manual of Mental Disorders, Third Edition
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
e-CHUG	Electronic Check-Up To Go
EBFT	Ecologically based family therapy
ED	Emergency department
Educ	psychoeducation
Fam	family focused therapy
FBT	family behavioral therapy
FDA	U.S. Food and Drug Administration
FES	Family Environment Scale
FFT	functional family therapy
FSN	family systems network
FST	family systems therapy
GED	General Equivalency Diploma

ICM	intensive case management
KQ	Key Question
LSS-A	Life Satisfaction Scale for Adolescents
MDFT	Multidimensional family therapy
MA	meta-analysis
MET	motivation enhancement therapy
MI	motivational interviewing
MST	Multi-systemic therapy
NAC	N-acetylcysteine
NMA	network meta-analysis
NMD	net mean difference
NIDA	National Institute of Drug Abuse
NOS	not otherwise specified
NRCS	nonrandomized comparative study
OR	odds ratio
PeerGroup	peer group therapy
PHYS	Parent Happiness with Youth Scale
PP	practice parameter
PPQ	Parenting Practices Questionnaire
PU	problematic use
RCT	randomized controlled trial
RR	risk ratio
SE	standard error
SIQ-JR	Suicidal Ideation Questionnaire for Adolescents
SMD	standardized mean difference
SR	systematic review
SRDR	Systematic Review Data Repository
STI	sexually transmitted infection
SUD	substance use disorder
T-ASI	Teen Addiction Severity Index
TAU	treatment as usual
TEP	Technical Expert Panel
YHPS	Youth Happiness with Parent Scale

Appendix A. Search Strategies

Primary Search for All Substances in Adolescents

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(((“Juvenile Delinquency/rehabilitation”[MeSH Terms] OR (juvenile AND (offender* or delinquency or prison)) OR ("Substance-Related Disorders"[Mesh] NOT ("Substance-Related Disorders/prevention and control"[Mesh] NOT "Substance-Related Disorders"[Mesh])) OR “drug offense” OR “Drug abuse” OR “drug misuse” OR “drug dependence” OR “drug addiction” OR “substance use” OR “substance abuse” OR “substance misuse” OR “substance dependence” OR “substance addiction” OR “prescription abuse” OR “Alcoholism”[Mesh] OR “cannabis use disorder” OR “alcohol use disorder” OR “stimulant use disorder” OR “hallucinogen use disorder” OR “opioid use disorder” OR “inhalant use disorder”) OR ((Alcohol OR “Alcoholic Beverages”[Mesh] OR cannabis OR Marijuana OR “Cannabis”[Mesh] OR “Marijuana Abuse”[Mesh] OR “Marijuana Smoking”[Mesh] OR opioids OR “Narcotics”[Mesh] OR “Analgesics, Opioid”[Mesh] OR kratom OR hallucinogens OR “Psychotropic Drugs”[Mesh] OR inhalants OR toluene OR ((amyl OR butyl OR isobutyl) AND nitrites) OR stimulants OR “Central Nervous System Stimulants”[Mesh] OR “Amphetamines”[Mesh] OR Sedatives OR “Hypnotics and Sedatives”[Mesh] OR Benzodiazepines OR “Benzodiazepines”[Mesh] OR Anthramycin OR Bromazepam OR Clonazepam OR Devazepide OR Diazepam OR Flumazenil OR Flunitrazepam OR Flurazepam OR Fentanyl OR Alprazolam OR Clonidine OR Hashish Clonidine OR Lorazepam OR Nitrazepam OR Oxazepam OR Pirenzepine OR Prazepam OR Temazepam OR Chlordiazepoxide OR Clorazepate Dipotassium OR Estazolam OR Medazepam OR Midazolam OR Triazolam OR opioid* OR opiate* OR Heroin OR opium OR “Morphine Derivatives”[Mesh] OR Codeine OR Hydrocodone OR Oxycodone OR Dihydromorphine OR Ethylmorphine OR Heroin OR Hydromorphone OR Morphine OR Oxymorphone OR Thebaine OR Cocaine OR “Cocaine”[Mesh] OR Methamphetamine* OR “Methamphetamine”[Mesh] OR Benzphetamine OR anabolic steroids OR “Testosterone Congeners”[Mesh] OR antihistamines OR nitrous oxide OR betel nut OR kava OR Ecstasy OR phenylalkylamines OR mescaline OR 2,5-dimethoxy-4-methylamphetamine OR MDMA OR 3,4-methylenedioxymethamphetamine OR indoleamine* OR psilocybin OR psilocin OR dimethyltryptamine OR ergoline* OR lysergic acid diethylamide OR “morning glory seeds” OR “Salvia divinorum” OR jimsonweed OR anxiolytic OR benzodiazepine* OR zolpidem OR zaleplon OR carbamate* OR glutethimide OR meprobamate OR barbiturate* OR secobarbital OR barbiturate* OR glutethimide OR methaqualone OR amphetamine OR dextroamphetamine OR methamphetamine OR gabapentin OR baclofen OR diacetylmorphine OR kratom OR polydrug OR “poly-drug” OR polysubstance OR “poly-substance” OR “injection drug”) AND (addict* OR abus* OR misus* OR disorder* OR mis-use OR dependen*)))

AND

("Telemedicine/methods"[Mesh] OR "Active aftercare" OR "Adolescent Community Reinforcement Approach" OR "Alcoholics Anonymous" OR "Narcotics Anonymous" OR "12-step" OR "assertive community treatment" OR "assertive continuing care" OR "Behavior Therapy"[Mesh] OR "brief intervention" OR "brief interventions" OR "Brief negotiated interview" OR "brief strategic family therapy" OR "Buprenorphine, Naloxone Drug Combination"[Mesh] OR "Buprenorphine"[Mesh] OR "Cognitive behavioral therapy" OR "Cognitive Therapy"[Mesh] OR "Cognitive-behavioral therapy" OR "Cognitive-behavioral treatment" OR "Combined Modality Therapy"[Mesh] OR "Contingency management" OR "Culturally Informed and Flexible Family-Based Treatment for Adolescents" OR "culturally-based intervention" OR "delinquency-treatment programs" OR "dopaminergic agent" OR "drug counseling" OR "Dual diagnosis therapy" OR "Dual diagnosis treatment" OR "Dual Recovery Therapy" OR "Family Therapy"[Mesh] OR "glutaminergic agent" OR "group therapy" OR "Harm reduction" OR "Interpersonal process groups" OR "Matrix-Model" OR "medication assisted treatment" OR "Methadone"[Mesh] OR "Motivational Enhancement Therapy" OR "Motivational incentives" OR "motivational interview" OR "motivational interviewing" OR "Motivational Interviewing"[Mesh] OR "Multidimensional Treatment Foster Care" OR "Multisystemic Therapy" OR "mutual help group" OR "Naloxone"[Mesh] OR "Narcotic Antagonists"[Mesh]) OR "Opioid replacement" OR "Opioid substitution" OR "oral THC" OR "Phoenix Academy" OR "Recovery Coach" OR "Recovery High School" OR "Reinforcement-based" OR "Seeking Safety" OR "Self-Help for Alcohol and Other Drug Use and Depression" OR "seven challenges" OR "Skills development groups" OR "Substance Abuse Program" OR "synthetic cannabinoids" OR "synthetic opioid" OR "systemic Therapy" OR "Teen Marijuana Check-Up" OR "Therapy, Computer-Assisted"[Mesh] OR ((family OR psychosocial OR Psychoeducational) and (therapy or therapies or treatment* or intervention* or counseling)) OR (behavior* AND (intervention* OR modification*)) OR A-CRA OR Acamprosate OR Acomplia OR amiodarone OR Buprenorphine OR Bupropion OR Cannabidiol OR CIFFTA OR citalopram OR dexamfetamine OR dexamphetamine OR Disulfiram OR duloxetine OR escitalopram OR fluoxetine OR gabapentin OR lisdexamfetamine OR Lithium OR Long-acting injectable OR meditation OR Methadone OR mindfulness OR Nabiximols OR Naltrexone OR paroxetine OR Peer-based OR "peer support" OR pemoline OR Pharmacological interventions OR prazosin OR pregabalin OR quetiapine OR Rimonabant OR Sativex OR SBIRT OR sertraline OR Topiramate OR varenicline OR venlafaxine OR Vilazodone)

AND

("Randomized Controlled Trial"[pt] OR "Cohort Studies"[Mesh] OR cohort OR "Clinical Trial" [Publication Type] OR longitudinal OR "Placebos"[Mesh] OR placebo* OR "Evaluation Studies" [Publication Type] OR "Comparative Study" [Publication Type] OR ((comparative or Intervention) AND study) OR pretest* OR preintervention OR posttest* OR prepost* OR "pre post" OR "before and after" OR interrupted time* OR time serie* OR ((quasi-experiment* OR quasiexperiment* OR quasi or experimental) and (method or study or trial or design*)) OR "Random Allocation"[Mesh] OR "Double-Blind Method"[Mesh] OR "Single-Blind Method"[Mesh] OR ((clinical OR controlled) and trial*) OR ((singl* or doubl* or trebl* or tripl*) and (blind* or mask*)) OR random*)

AND

(adolescent [MeSH] OR adolescen* OR teen* OR young people OR young person* OR young adult* OR youth* OR girl OR girls OR boy OR boys OR juvenile* OR "Young Adult"[Mesh]))

NOT

(((“adult”[mesh] OR "Infant"[Mesh] OR “child”[mesh]) NOT “adolescent”[mesh]) OR neonat* OR infant* OR “addresses”[pt] or “autobiography”[pt] or “bibliography”[pt] or “biography”[pt] or “case reports”[pt] or “comment”[pt] or “congresses”[pt] or “dictionary”[pt] or “directory”[pt] or “festschrift”[pt] or “government publications”[pt] or “historical article”[pt] or “interview”[pt] or “lectures”[pt] or “legal cases”[pt] or “legislation”[pt] or “news”[pt] or “newspaper article”[pt] or “patient education handout”[pt] or “periodical index”[pt] or "comment on" or ("Animals"[Mesh] NOT "Humans"[Mesh]) OR rats[tw] or cow[tw] or cows[tw] or chicken*[tw] or horse[tw] or horses[tw] or mice[tw] or mouse[tw] or bovine[tw] or sheep or ovine or murinae or “animal model”)

Cochrane last run on 10/31/19

ID Search Hits

#1 MeSH descriptor: [Substance-Related Disorders] explode all trees

#2 alcohol* or cannabis or marijuana or opioid* or narcotic* or hallucinogen* or psychotropic or stimulant* or opiate* or steroid* or polydrug or polysubstance or drug* or substance* or prescription

#3 addict* or abus* or misus* or mis-use or dependen*

#4 #2 NEAR #3

#5 #1 OR #4

#6 treatment or therapy or intervention or counseling

#7 #5 AND #6

#8 adolescen* or teen* or "young people" or "young person" or "young adult" or "young adults" or youth* or girl or girls or boy or boys or juvenile*

#9 #7 and #8

CINAHL/PsycINFO last run on 10/31/19

((alcohol* or cannabis or marijuana or opioid* or narcotic* or hallucinogen* or psychotropic or stimulant* or opiate* or steroid* or polydrug or polysubstance or drug* or substance* or prescription) N1 (addict* or abus* or misus* or mis-use or dependen*))

AND

(treatment or intervention or therapy or counseling)

AND

(adolescen* or teen* or "young people" or "young person" or "young adult" or "young adults" or youth* or girl or girls or boy or boys or juvenile*)

AND

("Randomized Controlled Trial" OR "Cohort Studies" OR cohort OR "Clinical Trial" OR longitudinal OR "Placebos" OR placebo* OR "Evaluation Studies" OR "Comparative Study" OR ((comparative or Intervention) AND study) OR pretest* OR preintervention OR posttest* OR prepost* OR "pre post" OR "before and after" OR interrupted time* OR time serie* OR ((quasi-experiment* OR quasiexperiment* OR quasi or experimental) and (method or study or trial or design*)) OR "Random Allocation" OR "Double-Blind Method" OR "Single-Blind Method" OR ((clinical OR controlled) and trial*) OR ((singl* or doubl* or trebl* or tripl*) and (blind* or mask*)) OR random*)

Limit to journals, adolescent, young adult

Embase last run on 10/31/19

#19
#4 AND #18 AND [embase]/lim AND ([article]/lim OR [article in press]/lim) AND ([adolescent]/lim OR [young adult]/lim) AND [humans]/lim
7289
#18
#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17

#17
'cohort analysis'/exp OR **'cohort analysis'**

#16
'longitudinal study'/exp OR **'longitudinal study'**

#15
'clinical study'/exp OR **'clinical study'**

#14
'prospective study'/exp OR **'prospective study'**

#13
randomly AND **allocated**

#12
'random allocation'

#11
'placebo'/de

#10
'crossover procedure'/de

#9
'double blind procedure'/de

#8
'single blind procedure'/de

#7
'randomization'/exp OR **'randomization'**

#6
'randomized controlled trial'/exp OR **'randomized controlled trial'**

#5
'clinical trial'/exp OR **'clinical trial'**

#4
#1 AND #2 AND #3 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim

#3
adolescen* OR **teen*** OR **'young people'** OR **'young person'** OR **'young adult'** OR **'young adults'** OR **youth*** OR **girl** OR **girls** OR **boy** OR **boys** OR **juvenile***

#2
treatment OR **therapy** OR **intervention** OR **counseling**

#1
'drug offense'/exp OR **'drug offense'** OR **'drug abuse'**/exp OR **'drug abuse'** OR **'drug misuse'**/exp OR **'drug misuse'** OR **'drug dependence'**/exp OR **'drug dependence'** OR **'drug addiction'**/exp OR **'drug addiction'** OR **'substance use'**/exp OR **'substance use'** OR **'substance abuse'**/exp OR **'substance abuse'** OR **'substance misuse'**/exp OR **'substance misuse'** OR **'substance dependence'**/exp OR **'substance dependence'** OR **'substance addiction'**/exp OR **'substance addiction'** OR **'prescription abuse'** OR **'alcoholism'**/exp OR **'alcoholism'** OR **'cannabis use disorder'**/exp OR **'cannabis use disorder'** OR **'alcohol use disorder'**/exp OR **'alcohol use disorder'** OR **'stimulant use disorder'** OR **'hallucinogen use disorder'** OR **'opioid use disorder'**/exp OR **'opioid use disorder'** OR **'inhalant use disorder'**

CT.gov last run 10/31/19

Substance Use OR Substance Abuse OR Drug Abuse OR drug dependence OR drug addiction OR prescription abuse OR Alcoholism OR cannabis OR alcohol OR stimulant OR hallucinogen OR opioid OR inhalant

adolescent OR teen OR young people OR young person OR young adult OR youth OR juvenile

Search for Systematic Reviews of Alcohol in College Settings

PubMed last run 10/31/19

("Alcoholism"[Mesh] OR "alcohol use disorder" OR "Alcohol Drinking"[Mesh] OR pregam* OR ((Alcohol* OR "Alcoholic Beverages"[Mesh] OR drink*) AND (addict* OR disorder* OR abus* OR misus* OR mis-use OR dependen* OR binge OR heavy OR problematic OR high-risk)))

AND

(colleg*[tiab] OR undergraduate*[tiab] OR "Universities"[Mesh] OR University[tiab] OR universities[tiab])

AND

(systematic[sb] OR meta-analysis[pt] OR meta-analysis as topic[mh] OR meta-analysis[mh] OR meta analy* OR metanaly* OR metaanaly* OR met analy* OR (systematic AND (review* OR overview*)) OR "Review Literature as Topic"[Mesh] OR Cochrane[tiab] OR embase[tiab] OR (psychlit[tiab] or psyclit[tiab]) OR (psycINFO[tiab] or psycinfo[tiab])OR (cinahl[tiab] or cinhal[tiab]) OR science citation index[tiab] OR bids[tiab] OR cancerlit[tiab] OR reference list*[tiab] OR bibliograph*[tiab] OR hand-search*[tiab] OR relevant journals[tiab] OR manual search*[tiab] OR selection criteria[tiab] OR data extraction[tiab])

Cochrane/Epistemonikos last run 10/31/19

(((Alcohol* OR drink*) AND (addict* OR disorder* OR abus* OR misus* OR mis-use OR dependen* OR binge OR heavy OR problematic OR high-risk)) OR pregam*)

AND

(colleg* OR undergraduate* OR University OR universities)

Appendix B. Excluded Studies

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
1	Abar	2015	26402351		Trajectories of Adolescent Alcohol Use in the Year Following a Brief Alcohol Intervention	No extractable or relevant data for interventions/outcomes of interest
2	Abdel-Salam	2014	2014-07010-005 (psychinfo)	10.3109/14659891.2012.728670	Examining the relationship between self-control and adolescent TC treatment completion	NRCS (nonpharm, pharmacological interventions N < 100)
3	Agosti	2007	L46871888 (embase)	10.1097/ADT.0b013e318059bb02	One-year posttreatment outcome of cannabis-dependent adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
4	Akhtar	2011	2011-11112-002 (psychinfo)	10.1921/095182410X576831	Applying positive psychology to alcohol-misusing adolescents: A group intervention	NRCS (nonpharm, pharmacological interventions N < 100)
5	Albornoz	2011	CN-00852012 (cochrane)		The effects of group improvisational music therapy on depression in adolescents and adults with substance abuse: a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
6	Alderson	2017	28536655	10.1186/s40814-017-0138-7	Supporting Looked After Children and Care Leavers In Decreasing Drugs, and alcohol (SOLID): protocol for a pilot feasibility randomised controlled trial of interventions to decrease risky substance use (drugs and alcohol) and improve mental health of looked after children and care leavers aged 12-20 years	No extractable or relevant data for interventions/outcomes of interest
7	Alizadehgoradel	2019	L2002789837 (Embase)	10.1016/j.npbr.2019.08.002	Mindfulness-based substance abuse treatment (MBSAT) improves executive functions in adolescents with substance use disorders	No extractable or relevant data for interventions/outcomes of interest
8	Andersson	2017	28028732	10.1007/s12529-016-9625-0	Interactive voice response with feedback intervention in outpatient treatment of substance use problems in adolescents and young adults: A randomized controlled trial	Includes transition-aged youth (non-pharmacological interventions)
9	Armitage	2014	24491079	10.1037/a0035802	A brief psychological intervention that reduces adolescent alcohol consumption	Not all subjects with at least problematic use

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
10	Arnaud	2012	23013141	10.1186/1471-2458-12-826	Web-based screening and brief intervention for poly-drug use among teenagers: study protocol of a multicentre two-arm randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
11	Arnaud	2015	26135277	10.1055/s-0034-1387681	Nachhaltiger Transfer des Gesundheitsnetz Alkohol im Jugendalter: Eine Kooperation aus Forschung, Praxis und Politik. = Sustainable transfer of the health network alcohol use in adolescence: A cooperation of research, practice and politics	No extractable or relevant data for interventions/outcomes of interest
12	Asdigian	2018	28032813	10.1080/00952990.2016.1265122	Effects of the 'Circle of Life' HIV-prevention program on marijuana use among American Indian middle school youths: a group randomized trial in a Northern Plains tribe	Not all subjects with at least problematic use
13	Azrin	1996	8561763		Follow-up results of supportive versus behavioral therapy for illicit drug use	RCT, N < 10 per arm
14	Babbin	2016	27082747	10.1016/j.addbeh.2016.03.033	Identifying treatment response subgroups for adolescent cannabis use	NRCS (nonpharm, pharmacological interventions N < 100)
15	Bacio	2017	28028740	10.1007/s11121-016-0741-5	Impact of Ethnic Composition on Mechanisms of Change in School-Based Substance Use Intervention Groups	Not all subjects with at least problematic use
16	Baer	2004	2004-18304-003 (psychinfo)	10.1080/1606635042000236475	Rationale and design of a brief substance use intervention for homeless adolescents	No extractable or relevant data for interventions/outcomes of interest
17	Bailey	2004	15370021	10.1080/09595230410001704136	Pilot randomized controlled trial of a brief alcohol intervention group for adolescents	Not all subjects with at least problematic use
18	Baldus	2011	21501479	10.1186/1472-6963-11-80	'CAN Stop'--implementation and evaluation of a secondary group prevention for adolescent and young adult cannabis users in various contexts--study protocol	No extractable or relevant data for interventions/outcomes of interest
19	Bamberg	2008	19004420	10.1080/02791072.2008.10400643	Including the siblings of youth substance abusers in a parent-focused intervention: a pilot test of the Best Plus program	NRCS (nonpharm, pharmacological interventions N < 100)
20	Bantchevska	2011	2011-23331-009 (psychinfo)	10.1093/swr/35.1.58	Predictors of drop-in center attendance among substance-abusing homeless adolescents	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
21	Barbosa	2018	29885153		Start-Up Costs of SBIRT Implementation for Adolescents in Urban U.S. Federally Qualified Health Centers	No extractable or relevant data for interventions/outcomes of interest
22	Barlow	2013	23409290	10.1176/appi.ajp.2012.12010121	Effect of a paraprofessional home-visiting intervention on American Indian teen mothers' and infants' behavioral risks: a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
23	Barnett	2002	2002-01321-003 (psychinfo)	10.1037/0893-164X.16.2.106	Predictors of motivation to change after medical treatment for drinking-related events in adolescents	No extractable or relevant data for interventions/outcomes of interest
24	Barnett	2010	20402989	10.1111/j.1360-0443.2009.02814.x	Moderators and mediators of two brief interventions for alcohol in the emergency department	Includes adults (> 25 years)
25	Bassett	2016	27211991	10.1016/j.jsat.2016.02.011	Evaluating Measures of Fidelity for Substance Abuse Group Treatment With Incarcerated Adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
26	Battjes	2004	15450645	10.1016/j.jsat.2004.06.002	Evaluation of a group-based substance abuse treatment program for adolescents	Single arm (nonpharm, pharmacological interventions N < 200)
27	Beach	2010	20954761	10.1037/a0020835	Differential susceptibility to parenting among African American youths: testing the DRD4 hypothesis	Not all subjects with at least problematic use
28	Becan	2015	25456094	10.1016/j.jsat.2014.10.002	Effectiveness of the Treatment Readiness and Induction Program for increasing adolescent motivation for change	NRCS (nonpharm, pharmacological interventions N < 100)
29	Becan	2018	29654518	10.1186/s40352-018-0068-3	A model for rigorously applying the Exploration, Preparation, Implementation, Sustainment (EPIS) framework in the design and measurement of a large scale collaborative multi-site study	Review
30	Becker	2012	22560729	10.1016/j.drugalcdep.2012.03.021	Trajectories of adolescent alcohol use after brief treatment in an Emergency Department	No extractable or relevant data for interventions/outcomes of interest
31	Becker	2017	28049542	10.1186/s13722-016-0067-4	Technology-assisted intervention for parents of adolescents in residential substance use treatment: protocol of an open trial and pilot randomized trial	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
32	Behar	1996	1996-02567-010 (psychinfo)	10.1007/BF02518648	Policy implications of the evaluation of the Fort Bragg child adolescent mental health demonstration project	No extractable or relevant data for interventions/outcomes of interest
33	Belur	2014	2014-08701-002 (psychinfo)	10.1080/1754730X.2014.888223	Feasibility and impact of implementing motivational enhancement therapy–cognitive behavioral therapy as a substance use treatment intervention in school-based settings	NRCS (nonpharm, pharmacological interventions N < 100)
34	Benarous	2016	2016-59773-001 (psychinfo)		Ecological momentary assessment and smartphone application intervention in adolescents with substance use and comorbid severe psychiatric disorders: Study protocol	No extractable or relevant data for interventions/outcomes of interest
35	Bergman	2015	26116368	10.1016/j.drugalcdep.2015.05.017	The effects of continuing care on emerging adult outcomes following residential addiction treatment	Single arm (nonpharm, pharmacological interventions N < 200)
36	Bernstein	2017	26999582	10.1097/PEC.0000000000000662	Reaching adolescents for prevention: The role of pediatric emergency department health promotion advocates	No extractable or relevant data for interventions/outcomes of interest
37	Bertholet	2012	22931392	10.1186/1471-2458-12-708	Predictive value of readiness, importance, and confidence in ability to change drinking and smoking	Not all subjects with at least problematic use
38	Bertholet	2016	27450907	10.1016/j.addbeh.2016.07.015	Are young men who overestimate drinking by others more likely to respond to an electronic normative feedback brief intervention for unhealthy alcohol use?	No extractable or relevant data for interventions/outcomes of interest
39	Bertholet	2018	29396897	10.1111/add.14179	Four-year follow-up of an internet-based brief intervention for unhealthy alcohol use in young men	Includes adults (> 25 years)
40	Bickman	1996	8694389		A continuum of care. More is not always better	No extractable or relevant data for interventions/outcomes of interest
41	Bohanna	2014	25082422	10.1136/bmjopen-2014-005689	A service-level action research intervention to improve identification and treatment of cannabis and related mental health issues in young Indigenous Australians: A study protocol	No extractable or relevant data for interventions/outcomes of interest
42	Bond	2004	15022372		Long-term impact of the Gatehouse Project on cannabis use of 16-year-olds in Australia	Not all subjects with at least problematic use

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
43	Boyd	2017	28583136	10.1186/s12954-017-0159-9	Social-structural factors influencing periods of injection cessation among marginalized youth who inject drugs in Vancouver, Canada: an ethno-epidemiological study	Review
44	Braciszewski	2018	29367098	10.1016/j.chiabu.2018.01.013	Developing a tailored substance use intervention for youth exiting foster care	Single arm (nonpharm, pharmacological interventions N < 200)
45	Branson		22332855	10.1111/j.1521-0391.2011.00204.x	A pilot study of low-cost contingency management to increase attendance in an adolescent substance abuse program	NRCS (nonpharm, pharmacological interventions N < 100)
46	Breda	2004	15230075	10.1081/ADA-120037377	Predicting incentives to change among adolescents with substance abuse disorder	No extractable or relevant data for interventions/outcomes of interest
47	Brody	2012	22157131	10.1542/peds.2011-0623	Family-centered program deters substance use, conduct problems, and depressive symptoms in black adolescents	Not all subjects with at least problematic use
48	Brody	2012	22182263	10.1037/a0026592	The Adults in the Making program: long-term protective stabilizing effects on alcohol use and substance use problems for rural African American emerging adults	Not all subjects with at least problematic use
49	Broome	2001	2002-02226-005 (psychinfo)	10.1177/0743558401166005	Engagement models for adolescents in DATOS-A	NRCS (nonpharm, pharmacological interventions N < 100)
50	Bryan	2009	19901006	10.1542/peds.2009-0679	HIV risk reduction among detained adolescents: a randomized, controlled trial	Review
51	Bryan	2018	29435591	10.1001/jamapediatrics.2017.5621	Effect of Including Alcohol and Cannabis Content in a Sexual Risk-Reduction Intervention on the Incidence of Sexually Transmitted Infections in Adolescents: A Cluster Randomized Clinical Trial	Not all subjects with at least problematic use
52	Buchan	2002	CN-00411895 (cochrane)		Cannabis use: consistency and validity of self-report, on-site urine testing and laboratory testing	No extractable or relevant data for interventions/outcomes of interest
53	Burleson	2006	17182415	10.1080/10550490601003656	Absence of iatrogenic or contagion effects in adolescent group therapy: findings from the Cannabis Youth Treatment (CYT) study	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
54	Burton	2007	16958129	10.1002/eat.20292	Experimental test of the affect-regulation theory of bulimic symptoms and substance use: a randomized trial	Not all subjects with at least problematic use
55	Callaghan	2007	17618062	10.1016/j.addbeh.2007.06.007	A case-matched comparison of readmission patterns between primary methamphetamine-using and primary cocaine-using adolescents engaged in inpatient substance abuse treatment	Review
56	Campos-Meledy	2017	27929303	10.1037/adb0000240	'The effect of therapists' adherence and competence in delivering the adolescent community reinforcement approach on client outcomes': Correction to Campos-Melady et al. (2016)	No extractable or relevant data for interventions/outcomes of interest
57	Carroll	2006	17032099	10.1037/0022-006X.74.5.955	The use of contingency management and motivational/skills-building therapy to treat young adults with marijuana dependence	Includes transition-aged youth (non-pharmacological interventions)
58	Cassidy	2019	31330464	10.1016/j.addbeh.2019.106044	Alcohol demand moderates brief motivational intervention outcomes in underage young adult drinkers	No extractable or relevant data for interventions/outcomes of interest
59	Caviness	2013	23795877	10.1111/j.1521-0391.2013.12030.x	Self-efficacy and motivation to quit marijuana use among young women	Case control/cross sectional
60	Chapman	2013	23668668	10.1037/a0033021	Comparison of youth, caregiver, therapist, trained, and treatment expert raters of therapist adherence to a substance abuse treatment protocol	No extractable or relevant data for interventions/outcomes of interest
61	Chassin	2009	18657942	10.1016/j.jsat.2008.06.001	Substance use treatment outcomes in a sample of male serious juvenile offenders	NRCS (nonpharm, pharmacological interventions N < 100)
62	Cheung	2013	2013-01351-014 (psychinfo)	10.1016/j.childyouth.2012.11.006	Reducing youth's drug abuse through training social workers for cognitive/havioral integrated treatment	Not all subjects with at least problematic use
63	Chi	2009	19344442	10.1111/j.1360-0443.2009.02524.x	Twelve-Step affiliation and 3-year substance use outcomes among adolescents: Social support and religious service attendance as potential mediators	Single arm (nonpharm, pharmacological interventions N < 200)
64	Christoff Ade	2015	25679364	10.1016/j.addbeh.2015.01.019	Reducing substance involvement in college students: a three-arm parallel-group randomized controlled trial of a computer-based intervention	Includes transition-aged youth (non-pharmacological interventions)
65	Chung	2008	18412757	10.1111/j.1360-0443.2008.02158.x	Cannabis withdrawal predicts severity of cannabis involvement at 1-year follow-up among treated adolescents	Single arm (nonpharm, pharmacological interventions N < 200)

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
66	Clark	2005	16139960	10.1016/j.addbeh.2005.07.017	Supervisory neglect and adolescent alcohol use disorders: effects on AUD onset and treatment outcome	NRCS (nonpharm, pharmacological interventions N < 100)
67	Clark	2010	19914003	10.1016/j.addbeh.2009.10.004	Project SUCCESS' effects on the substance use of alternative high school students	Not all subjects with at least problematic use
68	Clark	2014	25358829	10.1111/jcap.12095	Facilitating access to effective and appropriate care for youth with mild to moderate mental health concerns in New Zealand	Not all subjects with at least problematic use
69	Clingempeel	2008	18444724	10.1037/0002-9432.78.1.29	Beyond treatment effects: comorbid psychopathologies and long-term outcomes among substance-abusing delinquents	No extractable or relevant data for interventions/outcomes of interest
70	Coatsworth	2001	11676271		Brief Strategic Family Therapy versus community control: engagement, retention, and an exploration of the moderating role of adolescent symptom severity	Not all subjects with at least problematic use
71	Collier	2001	11696966	10.2190/GMC2-K3XX-XLHF-K2J0	The use of node-link mapping in the chemical dependency treatment of adolescents	No extractable or relevant data for interventions/outcomes of interest
72	Comulada	2015	26114764	10.1080/15332640.2014.986354	Compliance to Cell Phone-Based EMA among Latino Youth in Outpatient Treatment	No extractable or relevant data for interventions/outcomes of interest
73	Conrod	2006	17007600	10.1207/s15374424jccp3504_6	Efficacy of cognitive-behavioral interventions targeting personality risk factors for youth alcohol misuse	Not all subjects with at least problematic use
74	Conrod	2011	21500886	10.1037/a0022997	Long-term effects of a personality-targeted intervention to reduce alcohol use in adolescents	Not all subjects with at least problematic use
75	Conrod	2013	23344135	10.1001/jamapsychiatry.2013.651	Effectiveness of a selective, personality-targeted prevention program for adolescent alcohol use and misuse: a cluster randomized controlled trial	Not all subjects with at least problematic use
76	Copeland	2001	CN-00510570 (cochrane)		A randomized controlled trial of brief interventions for cannabis problems among young offenders	Review
77	Corbin	2013	23347236	10.1111/j.1530-0277.2012.01956.x	Early subjective response and acquired tolerance as predictors of alcohol use and related problems in a clinical sample	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
78	Cornelius	2005	15833583	10.1016/j.addbeh.2004.08.025	Fluoxetine in adolescents with comorbid major depression and an alcohol use disorder: a 3-year follow-up study	Single arm (nonpharm, pharmacological interventions N < 200)
79	Cornelius	2006	CN-00714147 (cochrane)		Alcohol use but not cannabis use reported to contribute to depression in treatment trial of comorbid adolescents	Review
80	Cornelius	2008	18313860	10.1016/j.addbeh.2008.02.001	Cannabis withdrawal is common among treatment-seeking adolescents with cannabis dependence and major depression, and is associated with rapid relapse to dependence	Single arm (nonpharm, pharmacological interventions N < 200)
81	Cornelius	2011	21530092	10.1016/j.addbeh.2011.03.016	Evaluation of cognitive behavioral therapy/motivational enhancement therapy (CBT/MET) in a treatment trial of comorbid MDD/AUD adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
82	Cornelius	2013	25904826		Paradoxical Decrease in Striatal Activation on an fMRI Reward Task Following Treatment in Youth with Co-morbid Cannabis Dependence/Major Depression	RCT, N < 10 per arm
83	Correia	2005	15561446	10.1016/j.addbeh.2004.04.006	Decreased substance use following increases in alternative behaviors: a preliminary investigation	College setting (alcohol interventions)
84	Cosden	2004	2005-03363-011 (psychinfo)	10.1007/BF03340912	Strength-Based Assessment of Adolescents Who Abuse Drugs: Implications for Helping High-Risk Youth	Single arm (nonpharm, pharmacological interventions N < 200)
85	Coulton	2017	28284187	10.1186/s12889-017-4170-6	Pragmatic randomised controlled trial to evaluate the effectiveness and cost effectiveness of a multi-component intervention to reduce substance use and risk-taking behaviour in adolescents involved in the criminal justice system: A trial protocol (RISKIT-CJS)	No extractable or relevant data for interventions/outcomes of interest
86	Cousins	2016	26234389	10.1111/add.13087	Risk of mortality on and off methadone substitution treatment in primary care: a national cohort study	NRCS (nonpharm, pharmacological interventions N < 100)
87	Cox	2006	16470234	10.1188/06.ONF.51-60	Predicting and modifying substance use in childhood cancer survivors: application of a conceptual model	Not all subjects with at least problematic use
88	Cunningham	1999	2000-15331-005 (psychinfo)	10.1023/A:1021951720298	Testing underlying assumptions of the family empowerment perspective	No extractable or relevant data for interventions/outcomes of interest
89	Cunningham	2012	22614776	10.1542/peds.2011-3419	Brief motivational interviewing intervention for peer violence and alcohol use in teens: one-year follow-up	Not all subjects with at least problematic use

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90	Cunningham	2012	CN-00845323 (cochrane)		One-year peer violence outcomes following a brief motivational interviewing intervention for violence and alcohol among teens	Review
91	Cunningham	2013	23758302	10.1111/acem.12151	Dating violence: outcomes following a brief motivational interviewing intervention among at-risk adolescents in an urban emergency department	Not all subjects with at least problematic use
92	Cunningham RM	2009	20053240	10.1111/j.1553-2712.2009.00513.x	Three-Month Follow-up Of Brief Computerized And Therapist	Not all subjects with at least problematic use
93	Curtis	2015	25757693	10.1080/19371918.2014.992713	The East Tennessee assertive adolescent family treatment program: a three-year evaluation	Single arm (nonpharm, pharmacological interventions N < 200)
94	D'Amico	2007	18072844	10.1037/0893-164X.21.4.592	Pilot test of Project CHOICE: a voluntary afterschool intervention for middle school youth	NRCS (nonpharm, pharmacological interventions N < 100)
95	D'Amico	2010	21113392	10.1080/07347324.2010.511076	Developing a group motivational interviewing intervention for first-time adolescent offenders at-risk for an alcohol or drug use disorder	Not all subjects with at least problematic use
96	D'Amico	2015	25365779	10.1037/a0038155	Group motivational interviewing for adolescents: Change talk and alcohol and marijuana outcomes	Single arm (nonpharm, pharmacological interventions N < 200)
97	D'Amico	2017	28627914	10.1037/adb0000288	Group motivational interviewing for homeless young adults: Associations of change talk with substance use and sexual risk behavior	Single arm (nonpharm, pharmacological interventions N < 200)
98	D'Amico	2018	30138016	10.1037/ccp0000332	Brief motivational interviewing intervention to reduce alcohol and marijuana use for at-risk adolescents in primary care.	Not all subjects with at least problematic use
99	D'Amico	2019	CN-01958806 (Cochrane)		Engaging at-risk ethnically diverse teens in four primary care settings in a clinical trial to reduce alcohol and marijuana use	No extractable or relevant data for interventions/outcomes of interest
100	D'Amico	2019	31296568	10.1542/peds.2018-3014	Understanding which teenagers benefit most from a brief primary care substance use intervention	Not all subjects with at least problematic use
101	D'Amico EJ	2016	27940696	10.1542/peds.2016-1717	Screening in Primary Care: What Is the Best Way to Identify At-Risk Youth for Substance Use?	Case control/cross sectional
102	D'Onofrio	2012	22459448	10.1016/j.annemergmed.2012.02.006	A brief intervention reduces hazardous and harmful drinking in emergency department patients	Includes transition-aged youth (non-pharmacological interventions)

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103	Daeppen	2011	20729010	10.1016/j.drugalcdep.2010.07.009	Efficacy of brief motivational intervention in reducing binge drinking in young men: a randomized controlled trial	Not all subjects with at least problematic use
104	Darnell	2015	25767310	10.1016/j.childyouth.2015.01.013	Quasi-Experimental Study of Functional Family Therapy Effectiveness for Juvenile Justice Aftercare in a Racially and Ethnically Diverse Community Sample	Not all subjects with at least problematic use
105	Dasinger	2004	15152707	10.1080/02791072.2004.10399721	Assessing the Effectiveness of Community-Based Substance Abuse Treatment for Adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
106	Davis	2013	24006963	10.1186/1472-6882-13-215	Pilot randomized trial on mindfulness training for smokers in young adult binge drinkers	Includes adults (> 25 years)
107	Davis	2016	26710670	10.1016/j.jsat.2015.10.004	Brief Motivational Interviewing and Normative Feedback for Adolescents: Change Language and Alcohol Use Outcomes	No extractable or relevant data for interventions/outcomes of interest
108	Davis	2016	27721646	10.1080/1067828X.2015.1056866	Informed assent recall among adolescents in substance use disorder treatment research	No extractable or relevant data for interventions/outcomes of interest
109	Davis	2018	29758380	10.1016/j.drugalcdep.2018.03.044	Predictors of positive drinking outcomes among youth receiving an alcohol brief intervention in the emergency department	No extractable or relevant data for interventions/outcomes of interest
110	Deady	2014	24583824	10.2196/resprot.3192	Evaluating a brief, internet-based intervention for co-occurring depression and problematic alcohol use in young people: protocol for a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
111	Deady	2016	27009465	10.2196/jmir.5178	An Online Intervention for Co-Occurring Depression and Problematic Alcohol Use in Young People: Primary Outcomes From a Randomized Controlled Trial	Includes transition-aged youth (non-pharmacological interventions)
112	Deluca	2015	25886178	10.1186/s12889-015-1679-4	Linked randomised controlled trials of face-to-face and electronic brief intervention methods to prevent alcohol related harm in young people aged 14-17 years presenting to Emergency Departments (SIPS junior)	No extractable or relevant data for interventions/outcomes of interest
113	DeMartini KS	2018	30138015	10.1037/ccp0000323	Drinking goals and attainment in a naltrexone trial of young adult heavy drinkers	No extractable or relevant data for interventions/outcomes of interest

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114	Dembo	1999	1999-05802-004 (psychinfo)	10.1016/S1359-1789(97)00028-1	Engaging high risk families in community based intervention services	Not all subjects with at least problematic use
115	Dembo	2000	CN-00688968 (cochrane)		A longitudinal study of the impact of a family empowerment intervention on juvenile offender psychosocial functioning: an expanded assessment	Not all subjects with at least problematic use
116	Dembo	2006	2006-08089-001 (psychinfo)	10.1300/J029v15n04_01	The Correlates and Consequences of Drug Involvement Among Youths Entering a Juvenile Justice Diversion Program	No extractable or relevant data for interventions/outcomes of interest
117	Dembo	2014	25400493	10.1080/1067828X.2014.928116	Brief Intervention for Truant Youth Sexual Risk Behavior and Marijuana Use	Not all subjects with at least problematic use
118	Dembo		27616873	10.1080/1067828X.2015.1103344	Impact of Brief Intervention Services on Drug-Using Truant Youths' Self-Reported Delinquency and Arrest Charges: A Longitudinal Study	Single arm (nonpharm, pharmacological interventions N < 200)
119	Dennis	2002	12460126		The Cannabis Youth Treatment (CYT) experiment: rationale, study design and analysis plans	No extractable or relevant data for interventions/outcomes of interest
120	Diamond	1999	2000-05929-004 (psychinfo)	10.1037/h0087729	Alliance-building interventions with adolescents in family therapy: A process study	NRCS (nonpharm, pharmacological interventions N < 100)
121	Diamond	2006	17182417	10.1080/10550490601003664	Early therapeutic alliance as a predictor of treatment outcome for adolescent cannabis users in outpatient treatment	No extractable or relevant data for interventions/outcomes of interest
122	Diamond	2006	2006-08089-002 (psychinfo)	10.1300/J029v15n04_02	Psychiatric Syndromes in Adolescents with Marijuana Abuse and Dependency in Outpatient Treatment	No extractable or relevant data for interventions/outcomes of interest
123	Diaz	2017	28704267	10.1097/MEJ.0000000000000488	Effect of a brief motivational intervention in reducing alcohol consumption in the emergency department: a randomized controlled trial	Includes transition-aged youth (non-pharmacological interventions)
124	Dick	2019	31500618	10.1186/s12889-019-7583-6	A systematic review of the effectiveness of digital interventions for illicit substance misuse harm reduction in third-level students	No extractable or relevant data for interventions/outcomes of interest

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125	Diestelkamp	2014	24975110	10.1186/1471-227X-14-13	Brief motivational intervention for adolescents treated in emergency departments for acute alcohol intoxication - a randomized-controlled trial	No extractable or relevant data for interventions/outcomes of interest
126	Diestelkamp	2016	27595811	10.13109/prkk.2016.65.7.534	[Influence of Counsellor- and Intervention Variables on Motivation to Change Following a Brief Motivational Intervention to Reduce Risky Alcohol Use]	No extractable or relevant data for interventions/outcomes of interest
127	Diestelkamp	2019	30670102	10.1186/s13063-018-3160-z	Effectiveness of a web-based screening and brief intervention with weekly text-message-initiated individualised prompts for reducing risky alcohol use among teenagers: Study protocol of a randomised controlled trial within the ProHEAD consortium	No extractable or relevant data for interventions/outcomes of interest
128	Donohue	1998	1999-10146-001 (psychinfo)	10.1300/J029v08n01_01	Improving initial session attendance of substance abusing and conduct disordered adolescents: A controlled study	NRCS (nonpharm, pharmacological interventions N < 100)
129	Doré-Gauthier	2019	30731429	10.1016/j.psychres.2019.01.076	How to help homeless youth suffering from first episode psychosis and substance use disorders? The creation of a new intensive outreach intervention team	Single arm (nonpharm, pharmacological interventions N < 200)
130	Douglas-Siegel	2013	23856594	10.1016/j.jsat.2013.05.010	The effect of recovery coaches for substance-involved mothers in child welfare: impact on juvenile delinquency	Not all subjects with at least problematic use
131	Doumas	2008	17600650	10.1016/j.jsat.2007.04.006	Preventing high-risk drinking in youth in the workplace: a web-based normative feedback program	Not all subjects with at least problematic use
132	Doumas	2014	24148137	10.1016/j.addbeh.2013.10.011	A test of the efficacy of a brief, web-based personalized feedback intervention to reduce drinking among 9th grade students	Not all subjects with at least problematic use
133	Doumas	2014	24666810	10.1016/j.jsat.2014.02.006	Reducing alcohol use among 9th grade students: 6 month outcomes of a brief, Web-based intervention	Not all subjects with at least problematic use
134	Doumas	2015	25448614	10.1016/j.jsat.2014.09.005	Web-based personalized feedback: Is this an appropriate approach for reducing drinking among high school students?	No extractable or relevant data for interventions/outcomes of interest
135	Doumas	2016	2016-50240-012 (psychinfo)	10.1080/1067828X.2016.1171185	Age of drinking initiation as a moderator of the efficacy of a brief, web-based personalized feedback alcohol intervention	Not all subjects with at least problematic use
136	Doumas	2017	28930058		A Randomized Controlled Trial Testing the Efficacy of a Brief Online Alcohol Intervention for High School Seniors	Not all subjects with at least problematic use

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137	Drost	2016	27103154	10.2196/jmir.5223	A Web-Based Computer-Tailored Alcohol Prevention Program for Adolescents: Cost-Effectiveness and Intersectoral Costs and Benefits	Not all subjects with at least problematic use
138	Dupont	2015	25990860	10.1186/s12889-015-1826-y	Developing the Moti-4 intervention, assessing its feasibility and pilot testing its effectiveness	Single arm (nonpharm, pharmacological interventions N < 200)
139	Dupont	2016	26780988	10.1016/j.jsat.2015.11.012	Assessing the Efficacy of MOTI-4 for Reducing the Use of Cannabis Among Youth in the Netherlands: A Randomized Controlled Trial	Includes transition-aged youth (non-pharmacological interventions)
140	Dupont		28548619	10.1080/02791072.2017.1325030	Stages of Change Model has Limited Value in Explaining the Change in Use of Cannabis among Adolescent Participants in an Efficacious Motivational Interviewing Intervention	Includes transition-aged youth (non-pharmacological interventions)
141	Dupouy		23337248	10.1016/j.jsat.2012.11.006	Effectiveness of drug tests in outpatients starting opioid substitution therapy	No extractable or relevant data for interventions/outcomes of interest
142	Easton	2012	22242558	10.3109/00952990.2011.643989	Differences in treatment outcome among marijuana-dependent young adults with and without antisocial personality disorder	Includes transition-aged youth (non-pharmacological interventions)
143	Edelen	2010	19819085	10.1016/j.drugalcdep.2009.09.008	Long-term effect of community-based treatment: evidence from the Adolescent Outcomes Project	Not all subjects with at least problematic use
144	Edwards	2006	16836598	10.1111/j.1600-0447.2006.00783.x	Randomized controlled trial of a cannabis-focused intervention for young people with first-episode psychosis	Includes adults (> 25 years)
145	Ellis	1979	500887		Delinquent drug takers: a follow up	NRCS (nonpharm, pharmacological interventions N < 100)
146	Engberg	2006	17156173	10.1111/j.1360-0443.2006.01544.x	Reducing substance use improves adolescents' school attendance	Single arm (nonpharm, pharmacological interventions N < 200)
147	Ewing	2014	24272742	10.1177/1078345813505445	Continued detention involvement and adolescent marijuana use trajectories	NRCS (nonpharm, pharmacological interventions N < 100)
148	Fagan	2006	2006-11654-002 (psychinfo)	10.1177/1066480706289651	Counseling and Treating Adolescents With Alcohol and Other Substance Use Problems and Their Families	Review

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149	Farrow	1999	CN-00159983 (cochrane)		Pregnant adolescents in chemical dependency treatment. Description and outcomes	Single arm (nonpharm, pharmacological interventions N < 200)
150	Faw	2004	CN-00476789 (cochrane)		Multidimensional fidelity evaluation in a residential program for adolescent substance abuse	Review
151	Feigelman		3443889	10.1080/02791072.1987.10472421	Day-care treatment for multiple drug abusing adolescents: Social factors linked with completing treatment	Single arm (nonpharm, pharmacological interventions N < 200)
152	Feldstein	2009	19298319	10.1111/j.1369-1600.2009.00149.x	Do genetic and individual risk factors moderate the efficacy of motivational enhancement therapy? Drinking outcomes with an emerging adult sample	College setting (alcohol interventions)
153	Fernández-Artamendi	2014	2016-25085-003 (psychinfo)	10.1016/j.ijchp.2014.04.001	Evidence-based treatments for adolescents with cannabis use disorders in the Spanish Public Health System	RCT, N < 10 per arm
154	Fernandes	2010	20385444	10.1016/j.addbeh.2010.03.001	Brief Motivational Intervention and telemedicine: a new perspective of treatment to marijuana users	Includes transition-aged youth (non-pharmacological interventions)
155	Fischer	2012	22538183	10.1186/1747-597X-7-15	12-month follow-up of an exploratory 'brief intervention' for high-frequency cannabis users among Canadian university students	Includes adults (> 25 years)
156	Fischer	2013	22520278	10.1016/j.jsat.2012.03.006	Feasibility and impact of brief interventions for frequent cannabis users in Canada	Includes adults (> 25 years)
157	Florsheim	2008	2008-15939-005 (psychinfo)	10.1007/s10964-007-9232-0	An experimental test of a craving management technique for adolescents in substance-abuse treatment	No extractable or relevant data for interventions/outcomes of interest
158	Forman	1990	CN-00346459 (cochrane)		Effects of coping skills training on adolescents at risk for substance use	Not all subjects with at least problematic use
159	Fors	1995	8907403	10.2190/TU92-LX8W-G7FD-9LEM	Evaluation of a peer-led drug abuse risk reduction project for runaway/homeless youths	NRCS (nonpharm, pharmacological interventions N < 100)
160	Fox	2011	21688873	10.1037/a0024331	Motives for cannabis use in high-risk adolescent users	No extractable or relevant data for interventions/outcomes of interest

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161	Freeborn	1995	7558471		Adolescent drug misuse treatment and use of medical care services	NRCS (nonpharm, pharmacological interventions N < 100)
162	Freedle	2015	2015-55090-009 (psychinfo)		The role of sandplay therapy in the treatment of adolescents and young adults with co-occurring substance use disorders and trauma	NRCS (nonpharm, pharmacological interventions N < 100)
163	French	2002	CN-00417055 (cochrane)		The economic cost of outpatient marijuana treatment for adolescents: findings from a multi-site field experiment	No extractable or relevant data for interventions/outcomes of interest
164	Freudenberg	2010	20970079	10.1016/j.jadohealth.2010.01.008	Reducing drug use, human immunodeficiency virus risk, and recidivism among young men leaving jail: evaluation of the REAL MEN re-entry program	Not all subjects with at least problematic use
165	Friedman	1986	3772356		Program characteristics for successful treatment of adolescent drug abuse	No extractable or relevant data for interventions/outcomes of interest
166	Friedman	2002	2002-04532-003 (psychinfo)	10.1300/J029v11n04_03	Multimodel substance use intervention program for male delinquents	Not all subjects with at least problematic use
167	Fromme		8040918		The Alcohol Skills Training Program: a group intervention for young adult drinkers	College setting (alcohol interventions)
168	Fulkerson	2008	18607698	10.1007/s10900-008-9117-5	Relationships between alcohol-related informal social control, parental monitoring and adolescent problem behaviors among racially diverse urban youth	Not all subjects with at least problematic use
169	Galai	2018	29966816	10.1016/j.socscimed.2018.06.013	A cluster randomized trial of community mobilization to reduce methamphetamine use and HIV risk among youth in Thailand: Design, implementation and results	Not all subjects with at least problematic use
170	Galaif	2001	2002-02226-008 (psychinfo)	10.1177/0743558401166008	Prospective risk factors and treatment outcomes among adolescents in DATOS-A	NRCS (nonpharm, pharmacological interventions N < 100)
171	Gantner	2006	17058778		[Multidimensional family therapy for adolescent clients with cannabis use disorders--Results and experience from the INCANT pilot study]	No extractable or relevant data for interventions/outcomes of interest

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172	Gantner	2006	2006-21027-002 (psychinfo)		Multidimensionale Familientherapie für cannabis-abhängige Jugendliche--Ergebnisse und Erfahrungen aus der 'INCANT'-Pilotstudie. = Multidimensional Family Therapy for adolescent clients with cannabis use disorders--Results and experience from the INCANT pilot study	No extractable or relevant data for interventions/outcomes of interest
173	Gantner		2010-11503-006 (psychinfo)	10.1024/0939-5911/a000002	Multidimensionale familientherapie (MDFT) in der praxis: Therapeutische erfahrungen mit jugendlichen cannabis-abhängigen und ihren familien. = Multidimensional family therapy in practice: Clinical experiences with adolescent cannabis abusers and their families	No extractable or relevant data for interventions/outcomes of interest
174	Garcia	2019	CN-01958827 (Cochrane)		Alcohol treatment response amonghispanic adolescents: a randomized trial	No extractable or relevant data for interventions/outcomes of interest
175	Gardner	2016	27296978	10.1016/j.drugalcdep.2016.05.018	Faster entry into HIV care among HIV-infected drug users who had been in drug-use treatment programs	No extractable or relevant data for interventions/outcomes of interest
176	Garner	2008	18472665	10.1080/02791072.2008.10399761	Predictors of early therapeutic alliance among adolescents in Substance abuse treatment	No extractable or relevant data for interventions/outcomes of interest
177	Garner	2009	18715742	10.1016/j.jsat.2008.06.007	Exposure to Adolescent Community Reinforcement Approach treatment procedures as a mediator of the relationship between adolescent substance abuse treatment retention and outcome	No extractable or relevant data for interventions/outcomes of interest
178	Garner	2010	20205824	10.1186/1748-5908-5-5	The Reinforcing Therapist Performance (RTP) experiment: study protocol for a cluster randomized trial	No extractable or relevant data for interventions/outcomes of interest
179	Garner	2012	22893231	10.1001/archpediatrics.2012.802	Using pay for performance to improve treatment implementation for adolescent substance use disorders: results from a cluster randomized trial	No extractable or relevant data for interventions/outcomes of interest
180	Garner	2014	25574502		Recovery Support for Adolescents with Substance use Disorders: The Impact of Recovery Support Telephone Calls Provided by Pre-Professional Volunteers	NRCS (nonpharm, pharmacological interventions N < 100)

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181	Garnick	2012	22364777	10.1016/j.drugalcdep.2012.01.011	The Washington circle engagement performance measures' association with adolescent treatment outcomes	Single arm (nonpharm, pharmacological interventions N < 200)
182	Gattamorta	2017	27849405	10.1080/10826084.2016.1229338	Psychiatric Symptoms, Parental Attachment, and Reasons for Use as Correlates of Heavy Substance Use Among Treatment-Seeking Hispanic Adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
183	Gattamorta		28661822	10.1080/15504263.2017.1343965	The Comorbidity of Psychiatric and Substance Use Disorders Among Hispanic Adolescents	Case control/cross sectional
184	Gau	2012	22414236	10.1080/16506073.2011.649781	Negative life events and substance use moderate cognitive behavioral adolescent depression prevention intervention	Not all subjects with at least problematic use
185	Gaume	2011	21777259	10.1111/j.1530-0277.2011.01526.x	Is brief motivational intervention effective in reducing alcohol use among young men voluntarily receiving it? A randomized controlled trial	Not all subjects with at least problematic use
186	Gaume	2014	24961378	10.1111/acer.12469	Influence of counselor characteristics and behaviors on the efficacy of a brief motivational intervention for heavy drinking in young men-a randomized controlled trial	Includes transition-aged youth (non-pharmacological interventions)
187	Geller	1992	CN-00185814 (cochrane)		Early findings from a pharmacokinetically designed double-blind and placebo-controlled study of lithium for adolescents comorbid with biporal and substance dependency disorders	RCT, N < 10 per arm
188	Geller	1992	1589586		Early findings from a pharmacokinetically designed double-blind and placebo-controlled study of lithium for adolescents comorbid with bipolar and substance dependency disorders	RCT, N < 10 per arm
189	Gil	2004	15488112	10.1111/j.1360-0443.2004.00861.x	Culturally sensitive substance abuse intervention for Hispanic and African American adolescents: empirical examples from the Alcohol Treatment Targeting Adolescents in Need (ATTAIN) Project	No extractable or relevant data for interventions/outcomes of interest
190	Gilder	2017	29021119	10.1016/j.jsat.2017.09.004	A pilot randomized trial of Motivational Interviewing compared to Psycho-Education for reducing and preventing underage drinking in American Indian adolescents	Not all subjects with at least problematic use
191	Giles	2016	28011807	10.1136/bmjopen-2016-012474	Multicentre individual randomised controlled trial of screening and brief alcohol intervention to prevent risky drinking in young people aged 14-15 in a high school setting (SIPS JR-HIGH): study protocol	No extractable or relevant data for interventions/outcomes of interest

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192	Gillespie	2017	28340901	10.1016/j.jsat.2017.01.001	Predictive validity of an observer-rated adherence protocol for multisystemic therapy with juvenile drug offenders	No extractable or relevant data for interventions/outcomes of interest
193	Gmel	2012	23089675	10.1007/s00038-012-0419-0	A quasi-randomized group trial of a brief alcohol intervention on risky single occasion drinking among secondary school students	NRCS (nonpharm, pharmacological interventions N < 100)
194	Gmel	2013	22885010	10.1016/j.jsat.2012.07.005	Effectiveness of a brief integrative multiple substance use intervention among young men with and without booster sessions	Not all subjects with at least problematic use
195	Godley	2004	15488111	10.1111/j.1360-0443.2004.00860.x	Thirty-month relapse trajectory cluster groups among adolescents discharged from out-patient treatment	No extractable or relevant data for interventions/outcomes of interest
196	Godley	2004	15152708	10.1080/02791072.2004.10399722	Comparing Outcomes of Best-Practice and Research-Based Outpatient Treatment Protocols for Adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
197	Godley	2005	15783279	10.1037/0893-164X.19.1.62	The stability and impact of environmental factors on substance use and problems after adolescent outpatient treatment for cannabis abuse or dependence	Single arm (nonpharm, pharmacological interventions N < 200)
198	Godley	2014	24294838	10.1037/a0035264	A randomized trial of assertive continuing care and contingency management for adolescents with substance use disorders	NRCS (nonpharm, pharmacological interventions N < 100)
199	Godley	2014	24462478	10.1016/j.jsat.2013.10.013	A comparison of treatment outcomes for adolescent community reinforcement approach participants with and without co-occurring problems	NRCS (nonpharm, pharmacological interventions N < 100)
200	Godley	2017	28282523	10.1016/j.drugalcdep.2016.12.029	Adolescent Community Reinforcement Approach implementation and treatment outcomes for youth with opioid problem use	NRCS (nonpharm, pharmacological interventions N < 100)
201	Goldbach	2011	2011-12055-003 (psychinfo)	10.1080/10538720.2011.560135	An examination of cultural adaptations performed by LGBT-identified youths to a culturally grounded, evidence-based substance abuse intervention	Review
202	Goldstein	2009	19858762	10.1097/CHI.0b013e3181bef6e8	Substance use and the treatment of resistant depression in adolescents	Not all subjects with at least problematic use

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
203	Gonzales	2008	19042326	10.1080/08897070802093312	An emerging problem	No extractable or relevant data for interventions/outcomes of interest
204	Gonzales	2014	24629885	10.1016/j.jsat.2014.01.010	Substance use recovery outcomes among a cohort of youth participating in a mobile-based texting aftercare pilot program	Includes transition-aged youth (non-pharmacological interventions)
205	Gonzales	2016	26689171	10.1111/ajad.12322	Youth recovery outcomes at 6 and 9 months following participation in a mobile texting recovery support aftercare pilot study	Includes transition-aged youth (non-pharmacological interventions)
206	Goorden	2016	27006273	10.1016/j.drugalcdep.2016.03.004	Cost-effectiveness of multidimensional family therapy compared to cognitive behavioral therapy for adolescents with a cannabis use disorder: Data from a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
207	Goti	2010	19779855	10.1007/s00787-009-0060-5	Brief intervention in substance-use among adolescent psychiatric patients: a randomized controlled trial	Not all subjects with at least problematic use
208	Grafsky	2011	21516226	10.1016/j.childyouth.2010.10.007	Comparison of treatment response among GLB and non-GLB street-living youth	No extractable or relevant data for interventions/outcomes of interest
209	Gray		16131498	10.1093/alcalc/agh199	The effectiveness of motivational interviewing delivered by youth workers in reducing drinking, cigarette and cannabis smoking among young people: quasi-experimental pilot study	NRCS (nonpharm, pharmacological interventions N < 100)
210	Grazioli	2015	25642586	10.1037/adb0000041	Protective behavioral strategies and future drinking behaviors: Effect of drinking intentions	No extractable or relevant data for interventions/outcomes of interest
211	Green	2007	17218647	10.1177/1077559506296317	How effective are family treatment drug courts? Outcomes from a four-site national study	Includes adults (> 25 years)
212	Gregor	2003	12883517		Feasibility of using an interactive laptop program in the emergency department to prevent alcohol misuse among adolescents	No extractable or relevant data for interventions/outcomes of interest
213	Grella	2001	11434639		Drug treatment outcomes for adolescents with comorbid mental and substance use disorders	NRCS (nonpharm, pharmacological interventions N < 100)

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
214	Grella	2003	12568501	10.1177/1077559502239610	Treatment processes and outcomes among adolescents with a history of abuse who are in drug treatment	No extractable or relevant data for interventions/outcomes of interest
215	Grenard	2007	17259065	10.1016/j.jadohealth.2006.08.008	Brief intervention for substance use among at-risk adolescents: a pilot study	NRCS (nonpharm, pharmacological interventions N < 100)
216	Grenier	1985	2991149		Treatment effectiveness in an adolescent chemical dependency treatment program: a quasi-experimental design	NRCS (nonpharm, pharmacological interventions N < 100)
217	Griffin	2012	22956890	10.1007/s10742-012-0089-7	Assessing the Sensitivity of Treatment Effect Estimates to Differential Follow-Up Rates: Implications for Translational Research	NRCS (nonpharm, pharmacological interventions N < 100)
218	Griffin	2014	24440050	10.1016/j.drugalcdep.2013.12.017	Estimating the causal effects of cumulative treatment episodes for adolescents using marginal structural models and inverse probability of treatment weighting	NRCS (nonpharm, pharmacological interventions N < 100)
219	Grossberg	2004	CN-00505912 (cochrane)		Brief physician advice for high-risk drinking among young adults	Includes adults (> 25 years)
220	Guo	2014	24364361	10.1037/a0035380	Reductions in depressive symptoms among substance-abusing runaway adolescents and their primary caretakers: a randomized clinical trial	No extractable or relevant data for interventions/outcomes of interest
221	Guo	2017	28426359	10.1080/10826084.2016.1267219	Reductions in Hard Drug Use Among Homeless Youth Receiving a Strength-Based Outreach Intervention: Comparing the Long-Term Effects of Shelter Linkage Versus Drop-in Center Linkage	Includes transition-aged youth (non-pharmacological interventions)
222	Guyll	2004	15222836	10.1037/0893-3200.18.2.293	Family-focused preventive interventions: evaluating parental risk moderation of substance use trajectories	Not all subjects with at least problematic use
223	Gwaltney	2011	21126827	10.1016/j.addbeh.2010.10.010	Using daily drinking data to characterize the effects of a brief alcohol intervention in an emergency room	Includes transition-aged youth (non-pharmacological interventions)
224	Hüsler	2005	15974138	10.1081/JA-200030560	The Action Plan--A New Instrument to Collect Data on Interventions in Secondary Prevention in Adolescents	Not all subjects with at least problematic use
225	Haastrup	1988	3348092		Eleven year follow-up of 300 young opioid addicts	Not all subjects with at least problematic use

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226	Hadland SE	2018	30208470	10.1001/jamapediatrics.2018.2143	Receipt of Timely Addiction Treatment and Association of Early Medication Treatment With Retention in Care Among Youths With Opioid Use Disorder	No extractable or relevant data for interventions/outcomes of interest
227	Hall	2014	24467198	10.1037/a0033845	Modeling motivation three ways: effects of MI metrics on treatment outcomes among adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
228	Haller	2014	24616136	10.1503/cmaj.131301	Effectiveness of training family physicians to deliver a brief intervention to address excessive substance use among young patients: a cluster randomized controlled trial	Not all subjects with at least problematic use
229	Hallfors	2006	16809591	10.2105/AJPH.2005.067462	Efficacy vs effectiveness trial results of an indicated 'model' substance abuse program: implications for public health	Not all subjects with at least problematic use
230	Halliday-Boykins	2010	20826076	10.1016/j.jsat.2010.07.011	Predicting nonresponse to juvenile drug court interventions	No extractable or relevant data for interventions/outcomes of interest
231	Hammond	2019	CN-01958416 (Cochrane)		Changes in psychiatric symptoms and opioid use during buprenorphine/naloxone treatment in opioid-dependent youth	No extractable or relevant data for interventions/outcomes of interest
232	Hammond	2019	CN-01961002 (Cochrane)		Association between opioid abstinence and anxious depression in opioid-dependent youth receiving short-term and extended buprenorphine/ naloxone-assisted treatment	No extractable or relevant data for interventions/outcomes of interest
233	Harris	2012	22566420	10.1542/peds.2011-1624	Computer-facilitated substance use screening and brief advice for teens in primary care: an international trial	Not all subjects with at least problematic use
234	Harrow	2006	16864469	10.1080/00952990600753677	The impact of publicly funded managed care on adolescent substance abuse treatment outcomes	Single arm (nonpharm, pharmacological interventions N < 200)
235	Hartzler	2017	28797270	10.1186/s13012-017-0633-5	Implementing the teen marijuana check-up in schools-a study protocol	No extractable or relevant data for interventions/outcomes of interest
236	Haug	2014	25099872	10.1186/1471-2458-14-809	Efficacy of a web- and text messaging-based intervention to reduce problem drinking in young people: study protocol of a cluster-randomised controlled trial	Not all subjects with at least problematic use

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
237	Haug	2017	27606700	10.1037/ccp0000138	Efficacy of a Web- and Text Messaging-Based Intervention to Reduce Problem Drinking in Adolescents: results of a Cluster-Randomized Controlled Trial	Not all subjects with at least problematic use
238	Haug	2017	29021116	10.1016/j.jsat.2017.09.008	Efficacy of a technology-based, integrated smoking cessation and alcohol intervention for smoking cessation in adolescents: results of a cluster-randomised controlled trial	Not all subjects with at least problematic use
239	Havard	2012	22014309	10.1111/j.1530-0277.2011.01632.x	Randomized controlled trial of mailed personalized feedback for problem drinkers in the emergency department: The short-term impact	Includes adults (> 25 years)
240	Haynes	2006	16676785		Sleep and aggression in substance-abusing adolescents: results from an integrative behavioral sleep-treatment pilot program	No extractable or relevant data for interventions/outcomes of interest
241	Helmer	2016	26969585	10.1186/s12889-016-2898-z	Development and evaluation of the efficacy of a web-based 'social norms'-intervention for the prevention and reduction of substance use in a cluster-controlled trial conducted at eight German universities	No extractable or relevant data for interventions/outcomes of interest
242	Henderson	2017	28745011	10.1111/eip.12458	Enhancing prevention and intervention for youth concurrent mental health and substance use disorders: The Research and Action for Teens study	NRCS (nonpharm, pharmacological interventions N < 100)
243	Henderson	2017	28167747	10.1136/bmjopen-2016-014080	Integrated collaborative care teams to enhance service delivery to youth with mental health and substance use challenges: protocol for a pragmatic randomised controlled trial	No extractable or relevant data for interventions/outcomes of interest
244	Henggeler	1991	CN-00241801 (cochrane)		Effects of multisystemic therapy on drug use and abuse in serious juvenile offenders: a progress report from two outcome studies	Not all subjects with at least problematic use
245	Herrington	1981	7343183		Alcohol and other drug dependence in adolescence: characteristics of those who seek treatment, and outcome of treatment	NRCS (nonpharm, pharmacological interventions N < 100)
246	Hides	2011	21806516		Does the addition of integrated cognitive behaviour therapy and motivational interviewing improve the outcomes of standard care for young people with comorbid depression and substance misuse?	NRCS (nonpharm, pharmacological interventions N < 100)
247	Hides	2013	23295899	10.1159/000341921	Quik Fix: a randomized controlled trial of an enhanced brief motivational interviewing intervention for alcohol/cannabis and psychological distress in young people	Includes transition-aged youth (non-pharmacological interventions)

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248	Hides	2014	25103779	10.1186/1471-227X-14-19	The Quik Fix study: a randomised controlled trial of brief interventions for young people with alcohol-related injuries and illnesses accessing emergency department and crisis support care	Includes transition-aged youth (non-pharmacological interventions)
249	Hides	2018	28992580	10.1016/j.addbeh.2017.09.020	Efficacy and outcomes of a mobile app targeting alcohol use in young people	Includes transition-aged youth (non-pharmacological interventions)
250	Hides		2007-01081-008 (psychinfo)		Young people with co-existing mental health and drug and alcohol problems	Review
251	Himelstein	2015	CN-01155528 (cochrane)		Does mindfulness meditation increase effectiveness of substance abuse treatment with incarcerated youth? A pilot randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
252	Hirschtritt	2012	22116008	10.1016/j.jsat.2011.09.010	Moderators of fluoxetine treatment response for children and adolescents with comorbid depression and substance use disorders	No extractable or relevant data for interventions/outcomes of interest
253	Hjorthøj	2013	23040144	10.1017/S0033291712002255	Specialized psychosocial treatment plus treatment as usual (TAU) versus TAU for patients with cannabis use disorder and psychosis: the CapOpus randomized trial	Includes adults (> 25 years)
254	Hoch	2012	21865014	10.1016/j.euroneuro.2011.07.014	Efficacy of a targeted cognitive-behavioral treatment program for cannabis use disorders (CANDIS)	Includes adults (> 25 years)
255	Hoeppner	2014	25150401	10.1016/j.drugalcdep.2014.07.023	Do young people benefit from AA as much, and in the same ways, as adult aged 30+? A moderated multiple mediation analysis	Includes adults (> 25 years)
256	Hoffman		8699540		Psychosocial treatments for cocaine abuse. 12-month treatment outcomes	Includes adults (> 25 years)
257	Hogue	2013	23314000	10.1016/j.evalprogplan.2012.12.001	Assessing fidelity to evidence-based practices in usual care: the example of family therapy for adolescent behavior problems	No extractable or relevant data for interventions/outcomes of interest
258	Hogue	2015	24711046	10.1007/s10488-014-0548-2	Validity of therapist self-report ratings of fidelity to evidence-based practices for adolescent behavior problems: correspondence between therapists and observers	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
259	Hops	2011	21833690	10.1007/s10461-011-0019-7	Adolescent health-risk sexual behaviors: effects of a drug abuse intervention	No extractable or relevant data for interventions/outcomes of interest
260	Horigian	2015	26359441	10.1111/ajad.12278	A cross-sectional assessment of the long term effects of brief strategic family therapy for adolescent substance use	Case control/cross sectional
261	Hser	2001	11448377		An evaluation of drug treatments for adolescents in 4 US cities	NRCS (nonpharm, pharmacological interventions N < 100)
262	Hser	2003	12770530		Drug-use initiation and conduct disorder among adolescents in drug treatment	NRCS (nonpharm, pharmacological interventions N < 100)
263	Huang	2011	20735217	10.3109/10826084.2010.501664	Effects of motivational enhancement therapy on readiness to change MDMA and methamphetamine use behaviors in Taiwanese adolescents	No extractable or relevant data for interventions/outcomes of interest
264	Huang	2014	24611528	10.1111/famp.12068	An application of the Complier Average Causal Effect analysis to examine the effects of a family intervention in reducing illicit drug use among high-risk Hispanic adolescents	Not all subjects with at least problematic use
265	Hunter	2012	22209657	10.1016/j.jsat.2011.11.003	The effectiveness of community-based delivery of an evidence-based treatment for adolescent substance use	NRCS (nonpharm, pharmacological interventions N < 100)
266	Hunter	2014	24128291	10.1037/a0034199	Longitudinal change mechanisms for substance use and illegal activity for adolescents in treatment	Single arm (nonpharm, pharmacological interventions N < 200)
267	Hunter	2014	2014-08701-003 (psychinfo)	10.1080/1754730X.2014.888224	Feasibility of implementing the Adolescent Community Reinforcement Approach in school settings for adolescents with substance use disorders	Single arm (nonpharm, pharmacological interventions N < 200)
268	Husted	1995	8555351		Multi-dimensional adolescent treatment with American Indians	Not all subjects with at least problematic use
269	Imel	2011	21534654	10.1037/a0023284	Racial/ethnic disparities in therapist effectiveness: A conceptualization and initial study of cultural competence	No extractable or relevant data for interventions/outcomes of interest
270	Ingels	2013	23998376	10.1016/j.drugalcdep.2013.07.036	Cost-effectiveness of the strong African American families-teen program: 1-year follow-up	Not all subjects with at least problematic use

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271	Jacobus	2018	29679914	10.1016/j.drugalcdep.2018.03.007	A multi-site proof-of-concept investigation of computerized approach-avoidance training in adolescent cannabis users	No extractable or relevant data for interventions/outcomes of interest
272	Jafari	2012	24644477		Comparing the effectiveness of Cognitive Behavioral Therapy and Stages of Change Model on Improving Abstinence Self-Efficacy in Iranian Substance Dependent Adolescents	No extractable or relevant data for interventions/outcomes of interest
273	Jaffee	2009	20180668	10.1080/00952990903150860	Methods of recruiting adolescents with psychiatric and substance use disorders for a clinical trial	No extractable or relevant data for interventions/outcomes of interest
274	Jalling		26900316	10.1007/s10826-015-0263-y	Parent Programs for Reducing Adolescent's Antisocial Behavior and Substance Use: A Randomized Controlled Trial	Not all subjects with at least problematic use
275	James	2011	L361167650 (embase)	10.1080/07347324.2011.538305	Characteristics of treatment completers versus treatment noncompleters in a targeted capacity expansion and HIV/AIDS education program for adolescents with substance use disorders	Single arm (nonpharm, pharmacological interventions N < 200)
276	James-Burdumy	2012	22265113	10.1016/j.jadohealth.2011.08.012	The effectiveness of mandatory-random student drug testing: a cluster randomized trial	Not all subjects with at least problematic use
277	Jander	2014	25301695	10.1186/1471-2458-14-1054	A Web-based computer-tailored game to reduce binge drinking among 16 to 18 year old Dutch adolescents: development and study protocol	No extractable or relevant data for interventions/outcomes of interest
278	Jander	2016	26842694	10.2196/jmir.4708	Effects of a Web-Based Computer-Tailored Game to Reduce Binge Drinking Among Dutch Adolescents: A Cluster Randomized Controlled Trial	No extractable or relevant data for interventions/outcomes of interest
279	Jaycox	2003	12921478	10.1097/01.CHI.0000046846.56865.F9	Mental health and medical problems and service use among adolescent substance users	NRCS (nonpharm, pharmacological interventions N < 100)
280	Johnson	2016	27770820	10.1186/s13063-016-1620-x	A randomised controlled trial of the clinical and cost-effectiveness of a contingency management intervention compared to treatment as usual for reduction of cannabis use and of relapse in early psychosis (CIRCLE): a study protocol for a randomised controlled trial	Includes adults (> 25 years)

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
281	Kaminer	2006	17182419	10.1080/10550490601006154	Suicidal ideation among adolescents with alcohol use disorders during treatment and aftercare	No extractable or relevant data for interventions/outcomes of interest
282	Kaminer	2014	25010430	10.1080/08897077.2014.933724	The efficacy of contingency management for adolescent cannabis use disorder: a controlled study	NRCS (nonpharm, pharmacological interventions N < 100)
283	Kaminer	2017	28232290	10.1016/j.addbeh.2017.02.013	Adolescents with cannabis use disorders: Adaptive treatment for poor responders	Single arm (nonpharm, pharmacological interventions N < 200)
284	Kaminer	2019	31403025	10.2174/2210676608666181102145040	Retention and treatment outcome of youth with cannabis use disorder referred by the legal system	Single arm (nonpharm, pharmacological interventions N < 200)
285	Kampman	2004	15283944	10.1016/j.drugalcdep.2004.03.008	A pilot trial of topiramate for the treatment of cocaine dependence	Includes adults (> 25 years)
286	Kay-Lambkin	2015	26444863	10.1186/s12889-015-2365-2	The iTreAD project: a study protocol for a randomised controlled clinical trial of online treatment and social networking for binge drinking and depression in young people	No extractable or relevant data for interventions/outcomes of interest
287	Kellogg	2006	16956865	10.1300/J069v25n03_03	Adolescent and young adult heroin patients: drug use and success in methadone maintenance treatment	NRCS (nonpharm, pharmacological interventions N < 100)
288	Kelly	2014	25294352	10.1093/alcalc/agu066	Do drug-dependent patients attending alcoholics anonymous rather than narcotics anonymous do aswell? A prospective, lagged, matching analysis	No extractable or relevant data for interventions/outcomes of interest
289	Kelly	2014	24945357	10.1371/journal.pone.0100121	Young adults, social networks, and addiction recovery: post treatment changes in social ties and their role as a mediator of 12-step participation	No extractable or relevant data for interventions/outcomes of interest
290	Kemp	2007	17852064	10.1080/10398560701439665	Stop Using Stuff: trial of a drug and alcohol intervention for young people with comorbid mental illness and drug and alcohol problems	RCT, N < 10 per arm
291	Kempf	1996	8703997	10.1300/J069v15n02_01	Impact of tobacco-free policy on recruitment and retention of adolescents in residential substance abuse treatment	Not all subjects with at least problematic use

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292	Kennedy		8411298		The Beech Hill Hospital/Outward Bound Adolescent Chemical Dependency Treatment Program	Single arm (nonpharm, pharmacological interventions N < 200)
293	Kim	2011	22004305	10.1037/a0025949	Substance use and delinquency among middle school girls in foster care: a three-year follow-up of a randomized controlled trial	Not all subjects with at least problematic use
294	Kim	2017	28523585	10.1007/s11121-017-0800-6	Pathways to Preventing Substance Use Among Youth in Foster Care	Not all subjects with at least problematic use
295	Kirby	1999	10462097		Community reinforcement training for family and significant others of drug abusers: a unilateral intervention to increase treatment entry of drug users	Includes adults (> 25 years)
296	Kirk	1990	1991-13660-001 (psychinfo)		Documenting the effectiveness of adolescent substance abuse treatment using public school archival records	No extractable or relevant data for interventions/outcomes of interest
297	Knight	2005	16026730	10.1016/j.jadohealth.2004.08.020	Motivational interviewing for adolescent substance use: a pilot study	Single arm (nonpharm, pharmacological interventions N < 200)
298	Knight	2015	24760288	10.1007/s10964-014-0127-6	Effectiveness of a theoretically-based judgment and decision making intervention for adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
299	Knight	2016	27130175	10.1186/s13012-016-0423-5	Juvenile Justice-Translational Research on Interventions for Adolescents in the Legal System (JJ-TRIALS): a cluster randomized trial targeting system-wide improvement in substance use services	No extractable or relevant data for interventions/outcomes of interest
300	Knight	2016	26742724	10.1016/j.jsat.2015.11.007	The Effectiveness of the Treatment Readiness and Induction Program (TRIP) for Improving During-Treatment Outcomes	NRCS (nonpharm, pharmacological interventions N < 100)
301	Knight	2018	29054734	10.1016/j.jadohealth.2017.08.013	Computer-Facilitated Screening and Brief Advice to Reduce Adolescents' Heavy Episodic Drinking: A Study in Two Countries	Single arm (nonpharm, pharmacological interventions N < 200)
302	Knight	2019	31225897	10.1001/jamanetworkopen.2019.6258	Effect of Computer-Based Substance Use Screening and Brief Behavioral Counseling vs Usual Care for Youths in Pediatric Primary Care: A Pilot Randomized Clinical Trial	Not all subjects with at least problematic use

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
303	Koning	2011	21496753	10.1016/j.amepre.2010.12.030	Long-term effects of a parent and student intervention on alcohol use in adolescents: a cluster randomized controlled trial	Not all subjects with at least problematic use
304	Koning	2014	24462480	10.1016/j.jsat.2013.11.003	Differential effects of baseline drinking status: effects of an alcohol prevention program targeting students and/or parents (PAS) among weekly drinking students	Not all subjects with at least problematic use
305	Kristiansen	2001	2002-02226-002 (psychinfo)	10.1177/0743558401166002	Methodological overview and research design for adolescents in the Drug Abuse Treatment Outcome Studies	Review
306	Kulis	2007	17096196	10.1007/s11121-006-0052-3	Promoting reduced and discontinued substance use among adolescent substance users: effectiveness of a universal prevention program	Not all subjects with at least problematic use
307	LaBrie	2015	25728042	10.1007/s11121-015-0549-8	The efficacy of a standalone protective behavioral strategies intervention for students accessing mental health services	College setting (alcohol interventions)
308	Lakshmana	2016	2016-52318-002 (psychinfo)	10.1080/1533256X.2016.1235414	Efficacy of combination of motivational interviewing and cognitive behavior intervention with substance abuse street adolescents in India: A randomized control study	No extractable or relevant data for interventions/outcomes of interest
309	Lammers	2015	25892544	10.1111/add.12952	Effectiveness of a selective intervention program targeting personality risk factors for alcohol misuse among young adolescents: results of a cluster randomized controlled trial	Not all subjects with at least problematic use
310	Lammers	2017	28282524	10.1016/j.addbeh.2017.02.030	Effectiveness of a selective alcohol prevention program targeting personality risk factors: Results of interaction analyses	Not all subjects with at least problematic use
311	Laporte	2014	24479702	10.1186/1745-6215-15-40	CANABIC: CANnabis and Adolescents: effect of a Brief Intervention on their Consumption--study protocol for a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
312	Laporte	2017	28289112	10.1370/afm.2003	Cannabis and Young Users-A Brief Intervention to Reduce Their Consumption (CANABIC): A Cluster Randomized Controlled Trial in Primary Care	Includes transition-aged youth (non-pharmacological interventions)
313	Larm P	2008	18375076	10.1016/j.drugalcdep.2008.01.026	Long-term outcomes of adolescents treated for substance misuse	Single arm (nonpharm, pharmacological interventions N < 200)

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314	Lascaux	2015	25526812	10.1016/j.encep.2014.10.013	[Comparison of European therapies for cannabis addiction among adolescents]	No extractable or relevant data for interventions/outcomes of interest
315	Latimer	2000	10860115		Demographic, individual, and interpersonal predictors of adolescent alcohol and marijuana use following treatment	NRCS (nonpharm, pharmacological interventions N < 100)
316	Lau-Barraco	2018	29485676	10.1111/acer.13606	A Randomized Trial of a Personalized Feedback Intervention for Nonstudent Emerging Adult At-Risk Drinkers	Includes transition-aged youth (non-pharmacological interventions)
317	Lecallier	2012	CN-00845229 (cochrane)		Screening, referring and counseling of adolescents for substance abuse. A randomized controlled study on 2120 students: reperer, orienter, conseiller les adolescents consommateurs de substances psycho-actives (ROC-ADO). etude prospective randomisee controlee aupres de 2120 adolescents	Not all subjects with at least problematic use
318	Lee	2010	20565152	10.1037/a0018859	A brief, web-based personalized feedback selective intervention for college student marijuana use: a randomized clinical trial	Not all subjects with at least problematic use
319	Lee	2015	25643024	10.1037/a0038792	A comparison of delay discounting in adolescents and adults in treatment for cannabis use disorders	No extractable or relevant data for interventions/outcomes of interest
320	Lee MJ	2013	23163605	10.1080/10810730.2012.727949	Underage drinkers' responses to negative-restrictive versus proactive-nonrestrictive slogans in humorous anti-alcohol abuse messages: are humorous responsible drinking campaign messages effective?	No extractable or relevant data for interventions/outcomes of interest
321	Lemma	2017	28551714	10.1007/s00213-017-4639-0	Cue avoidance training and inhibitory control training for the reduction of alcohol consumption: a comparison of effectiveness and investigation of their mechanisms of action	College setting (alcohol interventions)
322	LeNoue	2017	29064160	10.1111/ajad.12634	Marijuana commercialization and adolescent substance treatment outcomes in Colorado	NRCS (nonpharm, pharmacological interventions N < 100)
323	Leontieva	2005	16253794	10.1016/j.jcrc.2005.05.009	Readiness to change problematic drinking assessed in the emergency department as a predictor of change	Single arm (nonpharm, pharmacological interventions N < 200)

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
324	Letourneau		26413463	10.2174/22106766113036660002	Caregiver Involvement in Sexual Risk Reduction with Substance Using Juvenile Delinquents: Overview and Preliminary Outcomes of a Randomized Trial	No extractable or relevant data for interventions/outcomes of interest
325	Lewis	2012	22988494	10.1155/2012/235646	Consumer Feedback following Participation in a Family-Based Intervention for Youth Mental Health	No extractable or relevant data for interventions/outcomes of interest
326	Lewis	2018	29511966	10.1007/s11121-018-0879-4	Evaluating Personalized Feedback Intervention Framing with a Randomized Controlled Trial to Reduce Young Adult Alcohol-Related Sexual Risk Taking	Includes transition-aged youth (non-pharmacological interventions)
327	Libby	2005	16098679	10.1016/j.addbeh.2005.07.012	What came first, major depression or substance use disorder? Clinical characteristics and substance use comparing teens in a treatment cohort	No extractable or relevant data for interventions/outcomes of interest
328	Liddle	2002	CN-00384841 (cochrane)		A randomized Controlled Trial of Intensive Outpatient, Family-Based Therapy vs. Residential Drug Treatment for Co-Morbid Adolescent Substance Abusers	Review
329	Liddle	2011	20427547	10.1177/0306624X10366960	Implementation outcomes of Multidimensional Family Therapy-Detention to Community: a reintegration program for drug-using juvenile detainees	NRCS (nonpharm, pharmacological interventions N < 100)
330	Liddle		CN-00642423 (cochrane)		Multidimensional family therapy for severely impaired, dually diagnosed youth: a randomized comparing outpatient and residential treatment	Review
331	Lifrak	1997	9054806		Naltrexone for alcoholic adolescents	Single arm (nonpharm, pharmacological interventions N < 200)
332	Lin	2016	2016-48192-011 (psychinfo)	10.1080/16066359.2016.1178244	Trajectories of nonmedical use of prescription opioids among adolescents in primary care	No extractable or relevant data for interventions/outcomes of interest
333	Lindenberg	2002	12173165		Reducing substance use and risky sexual behavior among young, low-income, Mexican-American women: comparison of two interventions	Not all subjects with at least problematic use
334	Lintz	2019	31298564	10.1089/cap.2018.0178	Associations between School-Based Substance Use Treatment and Academic Outcomes	Single arm (nonpharm, pharmacological interventions N < 200)

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
335	Liu	2009	19288196	10.1007/s11121-009-0125-1	Evaluating mediation in longitudinal multivariate data: mediation effects for the Aban Aya Youth Project drug prevention program	Not all subjects with at least problematic use
336	Lloyd	1974	4430521		Evolution of a treatment approach for young heroin addicts. Comparison of three treatment modalities	NRCS (nonpharm, pharmacological interventions N < 100)
337	Lott	2009	19250774	10.1016/j.drugalcdep.2009.01.010	Effectiveness of very low-cost contingency management in a community adolescent treatment program	Single arm (nonpharm, pharmacological interventions N < 200)
338	Louis-Jacques	2014	24216313	10.1016/j.jadohealth.2013.09.012	Do risky friends change the efficacy of a primary care brief intervention for adolescent alcohol use?	NRCS (nonpharm, pharmacological interventions N < 100)
339	Luchansky	2006	16597576	10.1300/J069v25n01_11	Treatment readmissions and criminal recidivism in youth following participation in chemical dependency treatment	No extractable or relevant data for interventions/outcomes of interest
340	Luchansky	2007	17175402	10.1016/j.jsat.2006.06.007	Treatment response by primary drug of abuse: Does methamphetamine make a difference?	NRCS (nonpharm, pharmacological interventions N < 100)
341	Luehring-Jones	2017	28992377	10.1111/acer.13520	A Single Session of Attentional Bias Modification Reduces Alcohol Craving and Implicit Measures of Alcohol Bias in Young Adult Drinkers	No extractable or relevant data for interventions/outcomes of interest
342	Magill	2009	19371492		The role of marijuana use in brief motivational intervention with young adult drinkers treated in an emergency department	Includes transition-aged youth (non-pharmacological interventions)
343	Mahu	2015	26011508	10.1111/add.12991	Can cannabis use be prevented by targeting personality risk in schools? Twenty-four-month outcome of the adventure trial on cannabis use: a cluster-randomized controlled trial	Not all subjects with at least problematic use
344	Maio	2005	15795723	10.1016/j.annemergmed.2004.10.013	A randomized controlled trial of an emergency department-based interactive computer program to prevent alcohol misuse among injured adolescents	Not all subjects with at least problematic use
345	March	2009	CN-00726682 (cochrane)		Predictors of outcome in Buprenorphine treatment for opioid-dependent youth	Review
346	Marlatt	1993	1994-15124-001 (psychinfo)	10.1016/S0005-7894(05)80314-4	Harm reduction for alcohol problems: Moving beyond the controlled drinking controversy	Review

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347	Marlowe	2008	19192860		An effectiveness trial of contingency management in a felony preadjudication drug court	Includes transition-aged youth (non-pharmacological interventions)
348	Marsch	2004	CN-00462191 (cochrane)		Pharmacological and behavioral interventions for opioid-dependent adolescents: a randomized, controlled trial	Review
349	Marsiglia	2015	25416154	10.1007/s10935-014-0380-1	Long-term effects of the keepin' it REAL model program in Mexico: substance use trajectories of Guadalajara middle school students	Not all subjects with at least problematic use
350	Martínez	2008	2008-07457-006 (psychinfo)		Resultados preliminares del programa de intervenciÃ³n breve para adolescentes que inician el consumo de alcohol y otras drogas. = Preliminary study of a brief intervention program for adolescents who initiate alcohol and other drugs consumption	Single arm (nonpharm, pharmacological interventions N < 200)
351	Marvel	2009	19378646		Multidimensional family therapy HIV/STD risk-reduction intervention: an integrative family-based model for drug-involved juvenile offenders	No extractable or relevant data for interventions/outcomes of interest
352	Mason	2009	2009-04436-006 (psychinfo)	10.1080/10678280902724184	Brief substance abuse treatment with urban adolescents: A translational research study	NRCS (nonpharm, pharmacological interventions N < 100)
353	Mason	2018	29706169	10.1016/j.jsat.2018.03.002	A pilot trial of text-delivered peer network counseling to treat young adults with cannabis use disorder	Includes transition-aged youth (non-pharmacological interventions)
354	Mason MJ	2018	30265057	10.1037/adb0000403	Who responds best to text-delivered cannabis use disorder treatment? A randomized clinical trial with young adults	Includes transition-aged youth (non-pharmacological interventions)
355	Mathews	2007	18351179	10.2190/DE.37.4.d	An impact evaluation of two versions of a brief intervention targeting alcohol use and physical activity among adolescents	Not all subjects with at least problematic use
356	McCarthy	2010	21121492		Efficacy of a brief cognitive behavioral therapy program to reduce excessive drinking behavior among new recruits entering the Irish Navy: a pilot evaluation	Not all subjects with at least problematic use
357	McClure	2014	24720376	10.3109/00952990.2013.878718	Cigarette smoking during an N-acetylcysteine-assisted cannabis cessation trial in adolescents	No extractable or relevant data for interventions/outcomes of interest

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358	McCollister	2009	18172769	10.1007/s11414-007-9094-y	Estimating the differential costs of criminal activity for juvenile drug court participants: challenges and recommendations	No extractable or relevant data for interventions/outcomes of interest
359	McGillicuddy	2001	11239729		Development of a skill training program for parents of substance-abusing adolescents	RCT, N < 10 per arm
360	McKay	2014	25134073	10.1016/j.adolescence.2014.07.014	The differential impact of a classroom-based, alcohol harm reduction intervention, on adolescents with different alcohol use experiences: a multi-level growth modelling analysis	Not all subjects with at least problematic use
361	McMurran	1990	2310865		Evaluation of a self-help manual for young offenders who drink: a pilot study	NRCS (nonpharm, pharmacological interventions N < 100)
362	Mello	2018	29471849	10.1186/s13012-018-0725-x	Implementing Alcohol Misuse SBIRT in a National Cohort of Pediatric Trauma Centers-a type III hybrid effectiveness-implementation trial	No extractable or relevant data for interventions/outcomes of interest
363	Melnick	1997	9366969		Motivation and readiness for therapeutic community treatment among adolescents and adult substance abusers	No extractable or relevant data for interventions/outcomes of interest
364	Meredith LS	2018	29316897	10.1186/s12875-017-0689-y	Influence of mental health and alcohol or other drug use risk on adolescent reported care received in primary care settings.	Case control/cross sectional
365	Mertens		24899076	10.1093/alcalc/agu030	Effectiveness of nurse-practitioner-delivered brief motivational intervention for young adult alcohol and drug use in primary care in South Africa: a randomized clinical trial	Includes transition-aged youth (non-pharmacological interventions)
366	Milburn	2012	22443839	10.1016/j.jadohealth.2011.08.009	A family intervention to reduce sexual risk behavior, substance use, and delinquency among newly homeless youth	Not all subjects with at least problematic use
367	Millman	1978	283716		Therapeutic detoxification of adolescent heroin addicts	NRCS (nonpharm, pharmacological interventions N < 100)
368	Mitchell	2012	23786511	10.1111/j.1521-0391.2012.00299.x	Screening, brief intervention, and referral to treatment (SBIRT) for substance use in a school-based program: services and outcomes	NRCS (nonpharm, pharmacological interventions N < 100)

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369	Mitchell	2016	26297321	10.1016/j.jsat.2015.06.011	SBIRT Implementation for Adolescents in Urban Federally Qualified Health Centers	No extractable or relevant data for interventions/outcomes of interest
370	Mohammadkhani		2016-17978-003 (psychinfo)		Effectiveness of guided adolescent problem solving on craving, attitude toward drug abuse and coping strategies in adolescents with substance abuse	No extractable or relevant data for interventions/outcomes of interest
371	Moitra	2016	26636547	10.1002/da.22460	Reductions in cannabis use are associated with mood improvement in female emerging adults	Includes transition-aged youth (non-pharmacological interventions)
372	Molina	2007	17667481	10.1097/chi.0b013e3180686d96	Delinquent behavior and emerging substance use in the MTA at 36 months: prevalence, course, and treatment effects	Not all subjects with at least problematic use
373	Molina	2013	23452682	10.1016/j.jaac.2012.12.014	Adolescent substance use in the multimodal treatment study of attention-deficit/hyperactivity disorder (ADHD) (MTA) as a function of childhood ADHD, random assignment to childhood treatments, and subsequent medication	Not all subjects with at least problematic use
374	Montanaro	2015	26510775	10.2196/jmir.4377	Using Videogame Apps to Assess Gains in Adolescents' Substance Use Knowledge: New Opportunities for Evaluating Intervention Exposure and Content Mastery	Not all subjects with at least problematic use
375	Montgomery	2012	22743160	10.1016/j.drugalcdep.2012.05.033	Moderating effects of race in clinical trial participation and outcomes among marijuana-dependent young adults	Includes transition-aged youth (non-pharmacological interventions)
376	Monti	2007	17565560	10.1111/j.1360-0443.2007.01878.x	Motivational interviewing versus feedback only in emergency care for young adult problem drinking	Includes transition-aged youth (non-pharmacological interventions)
377	Moore	2009	19938941	10.1080/10826080802495229	Efficacy of a brief alcohol consumption reintervention for adolescents	Not all subjects with at least problematic use
378	Moore	2014	24041131	10.3109/10826084.2013.832328	'This is not who I want to be:' experiences of opioid-dependent youth before, and during, combined buprenorphine and behavioral treatment	No extractable or relevant data for interventions/outcomes of interest
379	Morehouse	2000	2000-07774-001 (psychinfo)		Preventing and reducing substance use among institutionalized adolescents	Not all subjects with at least problematic use

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380	Morgan-Lopez	2019	30981034	10.1016/j.addbeh.2019.04.006	A quasi-experimental evaluation of partnerships for success's impact on community-level ethanol and prescription drug poisoning rates	No extractable or relevant data for interventions/outcomes of interest
381	Morgenstern	2009	19207348	10.1111/j.1360-0443.2008.02471.x	School-based alcohol education: results of a cluster-randomized controlled trial	Not all subjects with at least problematic use
382	Morral	2004	15482081	10.1037/0893-164X.18.3.257	Effectiveness of community-based treatment for substance-abusing adolescents: 12-month outcomes of youths entering phoenix academy or alternative probation dispositions	NRCS (nonpharm, pharmacological interventions N < 100)
383	Motamed	2008	21768987	10.1097/ADM.0b013e31816b2f84	Differences in Treatment Outcomes between Prescription Opioid-Dependent and Heroin-Dependent Adolescents	No extractable or relevant data for interventions/outcomes of interest
384	Mun	2018	29229017	10.1017/S0954579417001742	Adolescence effortful control as a mediator between family ecology and problematic substance use in early adulthood: A 16-year prospective study	Not all subjects with at least problematic use
385	Murphy	2012	22191456	10.1089/apc.2011.0157	Alcohol and marijuana use outcomes in the Healthy Choices motivational interviewing intervention for HIV-positive youth	Includes transition-aged youth (non-pharmacological interventions)
386	Mustafaoglu	2019	31026384	10.1002/ppul.24330	Effects of core stabilization exercises on pulmonary function, respiratory muscle strength, and functional capacity in adolescents with substance use disorder: Randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
387	Myers	2008	19042327	10.1080/08897070802093361	Does smoking intervention influence adolescent substance use disorder treatment outcomes?	Not all subjects with at least problematic use
388	Naar-King	2006	16539572	10.1521/aeap.2006.18.1.1	Healthy choices: motivational enhancement therapy for health risk behaviors in HIV-positive youth	Includes transition-aged youth (non-pharmacological interventions)
389	Naar-King	2009	19996045	10.1001/archpediatrics.2009.212	Improving health outcomes for youth living with the human immunodeficiency virus: a multisite randomized trial of a motivational intervention targeting multiple risk behaviors	Not all subjects with at least problematic use
390	Needels	2005	16014874	10.1093/jurban/jti092	Community case management for former jail inmates: its impacts on rearrest, drug use, and HIV risk	NRCS (nonpharm, pharmacological interventions N < 100)

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391	Neighbors	2010	20409432		Cost-effectiveness of a motivational intervention for alcohol-involved youth in a hospital emergency department	No extractable or relevant data for interventions/outcomes of interest
392	Newcomb	2018	29332235	10.1007/s10461-018-2027-3	Do Diary Studies Cause Behavior Change? An Examination of Reactivity in Sexual Risk and Substance Use in Young Men Who Have Sex with Men	Includes adults (> 25 years)
393	Newton	2017	28801399	10.1136/bmjopen-2016-015423	A randomised controlled pilot trial evaluating feasibility and acceptability of a computer-based tool to identify and reduce harmful and hazardous drinking among adolescents with alcohol-related presentations in Canadian pediatric emergency departments	No extractable or relevant data for interventions/outcomes of interest
394	Newton	2018	29783974	10.1186/s12889-018-5554-y	Pathways to prevention: protocol for the CAP (Climate and Preventure) study to evaluate the long-term effectiveness of school-based universal, selective and combined alcohol misuse prevention into early adulthood	Not all subjects with at least problematic use
395	Niederhofer	2003	12544017	10.1097/01.ALC.0000047305.32374.FE	Tianeptine may be a useful adjunct in the treatment of alcohol dependence of adolescents	Review
396	Niederhofer	2003	12768462	10.1007/s00787-003-0327-1	Acamprosate and its efficacy in treating alcohol dependent adolescents	Retracted article
397	Nilsson	2004	2004-11429-004 (psychinfo)	10.1093/heapro/dah108	Evaluation of a health promotion programme to prevent the misuse of androgenic anabolic steroids among Swedish adolescents	Not all subjects with at least problematic use
398	Nirenberg	2013	23948537		Treatment may influence self-report and jeopardize our understanding of outcome	Not all subjects with at least problematic use
399	Noel	2006	16864466	10.1080/00952990500328646	The impact of therapeutic case management on participation in adolescent substance abuse treatment	Not all subjects with at least problematic use
400	Novins		22880543	10.1080/02791072.2012.684628	Walking on: celebrating the journeys of Native American adolescents with substance use problems on the winding road to healing	Review
401	O'Connor	2016	27219498	10.1111/acer.13111	Alcohol Intervention for Adolescents with Fetal Alcohol Spectrum Disorders: Project Step Up, a Treatment Development Study	NRCS (nonpharm, pharmacological interventions N < 100)
402	O'Leary-Barrett	2010	20732631	10.1016/j.jaac.2010.04.011	Personality-targeted interventions delay uptake of drinking and decrease risk of alcohol-related problems when delivered by teachers	Not all subjects with at least problematic use

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403	Ogborne	1997	9143643		Justice system clients of a Toronto youth addiction treatment program	No extractable or relevant data for interventions/outcomes of interest
404	Okulicz-Kozaryn	2012	22551472	10.1186/1471-2458-12-319	Effectiveness of the Strengthening Families Programme 10-14 in Poland for the prevention of alcohol and drug misuse: protocol for a randomized controlled trial	Not all subjects with at least problematic use
405	Oliansky	2009	CN-00198135 (cochrane)		Effectiveness of brief interventions in reducing substance use among at- risk primary care patients in three community-based clinics	Not all subjects with at least problematic use
406	Olmstead	2007	17645430	10.1111/j.1360-0443.2007.01909.x	The cost-effectiveness of four treatments for marijuana dependence	Includes transition-aged youth (non-pharmacological interventions)
407	Orlando	2003	12765210	10.1081/ADA-120020518	Retention of court-referred youths in residential treatment programs: Client characteristics and treatment process effects	No extractable or relevant data for interventions/outcomes of interest
408	Ozdemir	2016	26381442	10.1111/add.13177	Does promoting parents' negative attitudes to underage drinking reduce adolescents' drinking? The mediating process and moderators of the effects of the Orebro Prevention Programme	Not all subjects with at least problematic use
409	Ozechowski	2014	24512127	10.1037/a0035889	Empirical Bayes MCMC estimation for modeling treatment processes, mechanisms of change, and clinical outcomes in small samples	No extractable or relevant data for interventions/outcomes of interest
410	Palfai	2014	24845164	10.1016/j.addbeh.2014.04.025	Web-based screening and brief intervention for student marijuana use in a university health center: pilot study to examine the implementation of eCHECKUP TO GO in different contexts	Includes transition-aged youth (non-pharmacological interventions)
411	Palm	2016	27289105	10.1177/1403494816654047	Motivational interviewing does not affect risk drinking among young women: A randomised, controlled intervention study in Swedish youth health centres	Review
412	Pantin	2009	19834053	10.1097/PSY.0b013e3181bb2913	A randomized controlled trial of Familias Unidas for Hispanic adolescents with behavior problems	Not all subjects with at least problematic use
413	Parsons	2014	24364800	10.1037/a0035311	A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men	Includes transition-aged youth (non-pharmacological interventions)

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414	Patel	2018	29535906	10.7759/cureus.2033	Is Cannabis Use Associated With the Worst Inpatient Outcomes in Attention Deficit Hyperactivity Disorder Adolescents?	Case control/cross sectional
415	Paz Castro	2017	28371696	10.1016/j.addbeh.2017.03.013	Moderators of outcome in a technology-based intervention to prevent and reduce problem drinking among adolescents	Not all subjects with at least problematic use
416	Perrier-Menard	2017	28734153	10.1016/j.addbeh.2017.07.015	The impact of youth internalising and externalising symptom severity on the effectiveness of brief personality-targeted interventions for substance misuse: A cluster randomised trial	Not all subjects with at least problematic use
417	Peters	2012	22189052	10.1016/j.addbeh.2011.11.036	Co-occurring marijuana use is associated with medication nonadherence and nonplanning impulsivity in young adult heavy drinkers	Includes transition-aged youth (non-pharmacological interventions)
418	Pfarrwaller	2019	31330465	10.1016/j.addbeh.2019.106049	Excessive substance use screening to encourage behaviour change among young people in primary care: Pilot study in preparation for a randomized trial	Not all subjects with at least problematic use
419	Phan	2010	CN-00789450 (cochrane)	10.1016/j.amp.2009.12.013	A random clinical trial concerning the psychotherapy of adolescents addicted to cannabis	No extractable or relevant data for interventions/outcomes of interest
420	Phan	2010	2010-04145-013 (psychinfo)	10.1016/j.amp.2009.12.013	Un essai clinique randomisé sur la psychothérapie des adolescents dépendants au cannabis. = A random clinical trial concerning the psychotherapy of adolescents addicted to cannabis	No extractable or relevant data for interventions/outcomes of interest
421	Phan	2011	21749677	10.1186/1471-244X-11-110	European youth care sites serve different populations of adolescents with cannabis use disorder. Baseline and referral data from the INCANT trial	No extractable or relevant data for interventions/outcomes of interest
422	Phan		2011-08525-005 (psychinfo)		Aspect 'multidimensionnel' de la consommation problématique de drogue chez les adolescents. = 'Multidimensional' aspect of substance abuse in adolescents	Review
423	Pirskanen		17456127	10.1111/j.1525-1446.2007.00632.x	A formative evaluation to develop a school health nursing early intervention model for adolescent substance use	NRCS (nonpharm, pharmacological interventions N < 100)
424	Planken	2010	2010-17904-004 (psychinfo)		Effects of a 10-minutes peer education protocol to reduce binge drinking among adolescents during holidays	Not all subjects with at least problematic use

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425	Polsky	2010	20626379	10.1111/j.1360-0443.2010.03001.x	Cost-effectiveness of extended buprenorphine-naloxone treatment for opioid-dependent youth: data from a randomized trial	No extractable or relevant data for interventions/outcomes of interest
426	Prado	2012	22776441	10.1016/j.drugalcdep.2012.06.011	The efficacy of Familias Unidas on drug and alcohol outcomes for Hispanic delinquent youth: main effects and interaction effects by parental stress and social support	Not all subjects with at least problematic use
427	Prado	2013	23408280	10.1007/s11121-012-0326-x	Ecodevelopmental and intrapersonal moderators of a family based preventive intervention for Hispanic youth: a latent profile analysis	Not all subjects with at least problematic use
428	Prince	2019	31144836	10.1037/pha0000301	A Preliminary Test of a Brief Intervention to Lessen Young Adults' Cannabis Use: Episode-Level Smartphone Data Highlights the Role of Protective Behavioral Strategies and Exercise	Includes transition-aged youth (non-pharmacological interventions)
429	Rabbi M	2018	30021714	10.2196/resprot.9850	Toward Increasing Engagement in Substance Use Data Collection: Development of the Substance Abuse Research Assistant App and Protocol for a Microrandomized Trial Using Adolescents and Emerging Adults.	No extractable or relevant data for interventions/outcomes of interest
430	Ramchand	2011	21513674		Using a cross-study design to assess the efficacy of motivational enhancement therapy-cognitive behavioral therapy 5 (MET/CBT5) in treating adolescents with cannabis-related disorders	No extractable or relevant data for interventions/outcomes of interest
431	Ramchand	2015	25219932	10.1176/appi.ps.201300517	Provision of mental health services as a quality indicator for adolescent substance abuse treatment facilities	Single arm (nonpharm, pharmacological interventions N < 200)
432	Ramo	2018	29510223	10.1016/j.cct.2018.02.014	Using Facebook to address smoking and heavy drinking in young adults: Protocol for a randomized, controlled trial	No extractable or relevant data for interventions/outcomes of interest
433	Randall	2011	CN-00605980 (cochrane)		Adapting multisystemic therapy to treat adolescent substance abuse more effectively	Review
434	Rew	2017	27411974	10.1177/0193945916658861	An Intervention to Enhance Psychological Capital and Health Outcomes in Homeless Female Youths	NRCS (nonpharm, pharmacological interventions N < 100)
435	Rhoades	2013	24003300	10.1080/1067828X.2013.788887	MTFC for High Risk Adolescent Girls: A Comparison of Outcomes in England and the United States	Not all subjects with at least problematic use

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436	Richard		8749724		Effectiveness of adjunct therapies in crack cocaine treatment	Includes adults (> 25 years)
437	Richter	2012	22722516	10.1097/JCP.0b013e31825e213e	Efficacy and safety of levetiracetam for the prevention of alcohol relapse in recently detoxified alcohol-dependent patients: a randomized trial	Includes adults (> 25 years)
438	Riggs		CN-00367159 (cochrane)		Effects of pemoline on ADHD, antisocial behaviors and substance use in adolescents with conduct disorder and substance use disorder	Review
439	Rigter	2010	20380718	10.1186/1471-244X-10-28	INCANT: a transnational randomized trial of multidimensional family therapy versus treatment as usual for adolescents with cannabis use disorder	No extractable or relevant data for interventions/outcomes of interest
440	Riley	2008	18493858	10.1007/s11414-008-9111-9	Implementation of MET/CBT 5 for adolescents	No extractable or relevant data for interventions/outcomes of interest
441	Robbins	2010	22002455		Transporting clinical research to community settings: designing and conducting a multisite trial of brief strategic family therapy	Review
442	Robbins	2011	21261433	10.1037/a0022146	Therapist adherence in brief strategic family therapy for adolescent drug abusers	No extractable or relevant data for interventions/outcomes of interest
443	Rogers	2004	15048860	10.1002/bsl.558	Predictors of Treatment Outcome in Dually-Diagnosed Antisocial Youth: An Initial Study of Forensic Inpatients	No extractable or relevant data for interventions/outcomes of interest
444	Rohde	2001	11437018	10.1097/00004583-200107000-00014	Impact of comorbidity on a cognitive-behavioral group treatment for adolescent depression	Not all subjects with at least problematic use
445	Rohde	2012	22564206	10.1037/a0028269	Reduced substance use as a secondary benefit of an indicated cognitive-behavioral adolescent depression prevention program	Not all subjects with at least problematic use
446	Rohrbach		20655946	10.1016/j.ypmed.2010.07.016	One-year follow-up evaluation of the Project Towards No Drug Abuse (TND) dissemination trial	Not all subjects with at least problematic use
447	Roll	2006	16905197	10.1016/j.psychres.2005.12.003	Contingency management: schedule effects	Includes adults (> 25 years)

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448	Rosenberg	1972	5067456		Methadone use in adolescent heroin addicts	NRCS (nonpharm, pharmacological interventions N < 100)
449	Roten	2013	23261493	10.1016/j.addbeh.2012.11.003	Marijuana craving trajectories in an adolescent marijuana cessation pharmacotherapy trial	No extractable or relevant data for interventions/outcomes of interest
450	Roten	2015	25661990	10.1016/j.addbeh.2015.01.013	Cognitive performance in a placebo-controlled pharmacotherapy trial for youth with marijuana dependence	No extractable or relevant data for interventions/outcomes of interest
451	Rotheram-Borus	2016	26837624	10.1007/s10461-015-1262-0	Feasibility of Using Soccer and Job Training to Prevent Drug Abuse and HIV	Not all subjects with at least problematic use
452	Rounds-Bryant	1999	10548436		Drug abuse treatment outcome study of adolescents: a comparison of client characteristics and pretreatment behaviors in three treatment modalities	No extractable or relevant data for interventions/outcomes of interest
453	Rowe	2003	2003-02519-005 (psychinfo)		Family therapy for early adolescent substance abuse	No extractable or relevant data for interventions/outcomes of interest
454	Rowe	2004	15050090	10.1016/S0740-5472(03)00166-1	Impact of psychiatric comorbidity on treatment of adolescent drug abusers	No extractable or relevant data for interventions/outcomes of interest
455	Rowe	2013	23085040	10.1016/j.jsat.2012.08.225	Implementation fidelity of Multidimensional Family Therapy in an international trial	No extractable or relevant data for interventions/outcomes of interest
456	Rowland	2008	2014-27598-002 (psychinfo)	10.1080/15470650802071622	Sibling outcomes from a randomized trial of evidence-based treatments with substance abusing juvenile offenders	Not all subjects with at least problematic use
457	Rupp	2012	CN-00902300 (cochrane)		Cognitive remediation therapy during treatment for alcohol dependence	No extractable or relevant data for interventions/outcomes of interest
458	Russell	2018	28185103	10.1007/s11121-017-0751-y	PROSPER Intervention Effects on Adolescents' Alcohol Misuse Vary by GABRA2 Genotype and Age	Not all subjects with at least problematic use

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459	Salazar Garcia	2011	2012-03248-012 (psychinfo)		Intervenciones breves con adolescentes estudiantes rurales que consumen alcohol en exceso. = Brief interventions with adolescent rural students who drink alcohol in excess	NRCS (nonpharm, pharmacological interventions N < 100)
460	Saloner	2014	24613095	10.1016/j.jadohealth.2014.01.002	Explaining racial/ethnic differences in adolescent substance abuse treatment completion in the United States: A decomposition analysis	No extractable or relevant data for interventions/outcomes of interest
461	Sambrano	2005	16161731	10.1081/ADA-200068089	Understanding Prevention Effectiveness in Real-World Settings: The National Cross-Site Evaluation of High Risk Youth Programs	Not all subjects with at least problematic use
462	Santisteban	2003	12666468		Efficacy of brief strategic family therapy in modifying Hispanic adolescent behavior problems and substance use	Not all subjects with at least problematic use
463	Saxon	1996	8828247		Pre-treatment characteristics, program philosophy and level of ancillary services as predictors of methadone maintenance treatment outcome	Includes adults (> 25 years)
464	Schell	2005	16033496	10.1111/j.1475-6773.2005.00399.x	Dynamic Effects among Patients' Treatment Needs, Beliefs, and Utilization: A Prospective Study of Adolescents in Drug Treatment	NRCS (nonpharm, pharmacological interventions N < 100)
465	Schelleman-Offermans	2014	24210898	10.1016/j.jadohealth.2013.09.001	Preventing adolescent alcohol use: effects of a two-year quasi-experimental community intervention intensifying formal and informal control	Not all subjects with at least problematic use
466	Schijven	2015	26198744	10.1186/s12888-015-0563-1	Evaluating a selective prevention program for substance use and comorbid behavioral problems in adolescents with mild to borderline intellectual disabilities: Study protocol of a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
467	Schinke	2004	15376818		Reducing the risks of alcohol use among urban youth: Three-year effects of a computer-based intervention with and without parent involvement	Not all subjects with at least problematic use
468	Schmiege	2009	19170452	10.1037/a0014513	Randomized trial of group interventions to reduce HIV/STD risk and change theoretical mediators among detained adolescents	No extractable or relevant data for interventions/outcomes of interest
469	Schoenwald	1996	1996-07046-004 (psychinfo)	10.1007/BF02233864	Multisystemic therapy treatment of substance abusing or dependent adolescent offenders: Costs of reducing incarceration, inpatient, and residential placement	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
470	Schuler	2014	24650830		Effectiveness of treatment for adolescent substance use: is biological drug testing sufficient?	NRCS (nonpharm, pharmacological interventions N < 100)
471	Schulte	2010	2010-23527-002 (psychinfo)	10.1080/1067828X.2010.515877	Influencing adolescent social perceptions of alcohol use to facilitate change through a school-based intervention	Single arm (nonpharm, pharmacological interventions N < 200)
472	Schuman-Olivier	2014	24953168	10.1016/j.jsat.2014.04.006	Emerging adult age status predicts poor buprenorphine treatment retention	Review
473	Schwegler		CN-00309151 (cochrane)		Clinical detoxification of juvenile drug addicts - drug therapy with piracetam and doxepin	Review
474	Schwinn	2010	20553661	10.15288/jsad.2010.71.535	Preventing alcohol use among late adolescent urban youth: 6-year results from a computer-based intervention	Not all subjects with at least problematic use
475	Scott	1988	CN-00058610 (cochrane)		Impact of fitness training on native adolescents' self-evaluations and substance use	NRCS (nonpharm, pharmacological interventions N < 100)
476	Sealock	1997	CN-00392595 (cochrane)		Drug treatment for juvenile offenders: some good and bad news	NRCS (nonpharm, pharmacological interventions N < 100)
477	Segatto	2011	21971774		Brief motivational interview and educational brochure in emergency room settings for adolescents and young adults with alcohol-related problems: a randomized single-blind clinical trial	Includes transition-aged youth (non-pharmacological interventions)
478	Segrott	2014	24438460	10.1186/1471-2458-14-49	Preventing substance misuse: study protocol for a randomised controlled trial of the Strengthening Families Programme 10-14 UK (SFP 10-14 UK)	No extractable or relevant data for interventions/outcomes of interest
479	Selnow	1985	3831285	10.2190/BBA3-FE34-M9UH-WNA3	Using a stratified approach in substance intervention and prevention programs among adolescents: an empirical analysis	No extractable or relevant data for interventions/outcomes of interest
480	Serafini	2018	2018-11974-005 (psychinfo)	10.1080/16066359.2017.1342819	Perceived parental support and adolescent motivation for substance use change: A preliminary investigation	NRCS (nonpharm, pharmacological interventions N < 100)
481	Sevy	2011	21636134	10.1016/j.psychres.2011.05.001	Olanzapine vs. risperidone in patients with first-episode schizophrenia and a lifetime history of cannabis use disorders: 16-week clinical and substance use outcomes	Includes adults (> 25 years)

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
482	Sexton	2010	20545407	10.1037/a0019406	The effectiveness of functional family therapy for youth with behavioral problems in a community practice setting	Not all subjects with at least problematic use
483	Shakeshaft	2014	24618831	10.1371/journal.pmed.1001617	The Effectiveness of Community Action in Reducing Risky Alcohol Consumption and Harm: a Cluster Randomised Controlled Trial	Not all subjects with at least problematic use
484	Shane	2006	17182418	10.1080/10550490601003714	Impact of Victimization on Substance Abuse Treatment Outcomes for Adolescents in Outpatient and Residential Substance Abuse Treatment	No extractable or relevant data for interventions/outcomes of interest
485	Sharp		9218237		Facilitation of internal locus of control in adolescent alcoholics through a brief biofeedback-assisted autogenic relaxation training procedure	No extractable or relevant data for interventions/outcomes of interest
486	Sheidow	2012	22389577	10.1080/1067828X.2012.636701	Money Matters: Cost Effectiveness of Juvenile Drug Court with and without Evidence-Based Treatments	No extractable or relevant data for interventions/outcomes of interest
487	Sheidow	2019	31393146	10.1037/adb0000497	Capacity of Juvenile Probation Officers in Low-Resourced, Rural Settings to Deliver an Evidence-Based Substance Use Intervention to Adolescents	No extractable or relevant data for interventions/outcomes of interest
488	Sherman	2009	CN-01601907 (cochrane)		Evaluation of a peer network intervention trial among young methamphetamine users in Chiang Mai, Thailand	Includes transition-aged youth (non-pharmacological interventions)
489	Shetgiri	2011	CN-00845424 (cochrane)		A randomized, controlled trial of a school-based intervention to reduce violence and substance use in predominantly Latino high school students	Not all subjects with at least problematic use
490	Shift	2001	CN-00367166 (cochrane)		Adolescent cannabis check-up and intervention trial	Review
491	Sinha		14504024		Engaging young probation-referred marijuana-abusing individuals in treatment: a pilot trial	Includes transition-aged youth (non-pharmacological interventions)
492	Slesnick	2004	18607515	10.1300/J020v22n02_02	Office versus home-based family therapy for runaway, alcohol abusing adolescents: examination of factors associated with treatment attendance	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
493	Slesnick	2005	CN-00591039 (cochrane)		Outcome of CRA with Homeless Adolescents: preliminary findings	Review
494	Slesnick	2006	16933433		Predictors of substance use and family therapy outcome among physically and sexually abused runaway adolescents	No extractable or relevant data for interventions/outcomes of interest
495	Slesnick	2006	16564644	10.1016/j.addbeh.2006.02.006	Primary alcohol versus primary drug use among adolescents: an examination of differences	No extractable or relevant data for interventions/outcomes of interest
496	Slesnick	2011	2011-00923-005 (psychinfo)	10.1111/j.1467-6427.2010.00530.x	Predictors of treatment attendance among adolescent substance abusing runaways: A comparison of family and individual therapy modalities	No extractable or relevant data for interventions/outcomes of interest
497	Slesnick	2013	24011094	10.1016/j.adolescence.2013.06.007	Two-year predictors of runaway and homeless episodes following shelter services among substance abusing adolescents	No extractable or relevant data for interventions/outcomes of interest
498	Slice	1998	L28294380 (embase)	10.1037/0893-164X.12.2.136	Relations of delinquency to adolescent substance use and problem use: A prospective study	Single arm (nonpharm, pharmacological interventions N < 200)
499	Smeerdijk	2014	24157087	10.1016/j.jsat.2013.09.006	Feasibility of teaching motivational interviewing to parents of young adults with recent-onset schizophrenia and co-occurring cannabis use	Includes adults (> 25 years)
500	Smeerdijk	2015	25959502	10.1017/S0033291715000793	Motivational interviewing and interaction skills training for parents of young adults with recent-onset schizophrenia and co-occurring cannabis use: 15-month follow-up	Includes adults (> 25 years)
501	Smith	2010	20953309	10.1080/1067828X.2010.511986	Preliminary Support for Multidimensional Treatment Foster Care in Reducing Substance Use in Delinquent Boys	Not all subjects with at least problematic use
502	Smith	2011	21831564	10.1016/j.jsat.2011.06.003	Adolescent Community Reinforcement Approach outcomes differ among emerging adults and adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
503	Smith	2014	23994049	10.1016/j.jsat.2013.07.004	Drug refusal skills training does not enhance outcomes of African American adolescents with substance use problems	NRCS (nonpharm, pharmacological interventions N < 100)

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504	Smith	2015	26877622	10.1177/1049731514535851	Normative Feedback and Adolescent Readiness to Change: A Small Randomized Trial	No extractable or relevant data for interventions/outcomes of interest
505	Smyth	2018	26800851	10.1111/eip.12318	Changes in psychological well-being among heroin-dependent adolescents during psychologically supported opiate substitution treatment	NRCS (nonpharm, pharmacological interventions N < 100)
506	Spaeth	2010	20515209	10.1037/a0019550	Examining the differential effectiveness of a life skills program (IPSY) on alcohol use trajectories in early adolescence	Not all subjects with at least problematic use
507	Spirito	2017	28259500	10.1016/j.jsat.2017.02.002	Effects of a brief, parent-focused intervention for substance using adolescents and their sibling	Not all subjects with at least problematic use
508	Stanczak	1973	4808169		Treatment of young suburban heroin addicts two and a half years later	Single arm (nonpharm, pharmacological interventions N < 200)
509	Stanforth	2016	27776675	10.1016/j.jsat.2016.08.005	Structure of Problem Recognition Questionnaire with Hispanic/Latino Adolescents	No extractable or relevant data for interventions/outcomes of interest
510	Stanger	2012	22182419	10.1037/a0026543	Delay discounting predicts adolescent substance abuse treatment outcome	No extractable or relevant data for interventions/outcomes of interest
511	Stanger	2019	31246068	10.1037/adb0000480	Working Memory Training and High Magnitude Incentives for Youth Cannabis Use: A SMART Pilot Trial	Includes transition-aged youth (non-pharmacological interventions)
512	Stanton	2004	15466681	10.1001/archpedi.158.10.947	Randomized trial of a parent intervention: parents can make a difference in long-term adolescent risk behaviors, perceptions, and knowledge	Not all subjects with at least problematic use
513	Stein	2006	20617117		Enhancing Substance Abuse Treatment Engagement in Incarcerated Adolescents	No extractable or relevant data for interventions/outcomes of interest
514	Stein	2011	21185685	10.1016/j.jsat.2010.11.001	A brief marijuana intervention for non-treatment-seeking young adult women	Includes transition-aged youth (non-pharmacological interventions)

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515	Stein	2014	25127289	10.1080/08897077.2014.949337	Measuring behaviors of individual adolescents during group-based substance abuse intervention	No extractable or relevant data for interventions/outcomes of interest
516	Stein	2018	28865169	10.1111/add.14026	A developmental-based motivational intervention to reduce alcohol and marijuana use among non-treatment-seeking young adults: a randomized controlled trial	Includes transition-aged youth (non-pharmacological interventions)
517	Stein MD	2014	24439950	10.1016/j.whi.2013.10.005	Alcohol use potentiates marijuana problem severity in young adult women.	Single arm (nonpharm, pharmacological interventions N < 200)
518	Stephenson	2018	29712625	10.2196/resprot.9414	Intervention to Increase HIV Testing Among Substance-Using Young Men Who Have Sex With Men: Protocol for a Randomized Controlled Trial	No extractable or relevant data for interventions/outcomes of interest
519	Sterling	2005	2005-05432-015 (psychinfo)	10.1097/01.ALC.0000164373.89061.2C	Chemical Dependency and Psychiatric Services for Adolescents in Private Managed Care: Implications for Outcomes	Single arm (nonpharm, pharmacological interventions N < 200)
520	Sterling	2009	19413644	10.1111/j.1530-0277.2009.00972.x	Three-year chemical dependency and mental health treatment outcomes among adolescents: the role of continuing care	NRCS (nonpharm, pharmacological interventions N < 100)
521	Sterling	2015	26523821	10.1001/jamapediatrics.2015.3145	Implementation of Screening, Brief Intervention, and Referral to Treatment for Adolescents in Pediatric Primary Care: A Cluster Randomized Trial	No extractable or relevant data for interventions/outcomes of interest
522	Sterling	2017	29021115	10.1016/j.jsat.2017.09.005	Specialty addiction and psychiatry treatment initiation and engagement: Results from an SBIRT randomized trial in pediatrics	No extractable or relevant data for interventions/outcomes of interest
523	Sterling	2018	29396080	10.1016/j.jadohealth.2017.10.016	Pediatrician and Behavioral Clinician-Delivered Screening, Brief Intervention and Referral to Treatment: Substance Use and Depression Outcomes	Not all subjects with at least problematic use
524	Sterling	2019	31018988	10.1542/peds.2018-2803	Health care use over 3 years after adolescent SBIRT	Not all subjects with at least problematic use
525	Stevens	2004	15152706	10.1080/02791072.2004.10399720	Gender Differences in Substance Use, Mental Health, and Criminal Justice: Involvement of Adolescents at Treatment Entry and at Three, Six, Twelve and Thirty Month Follow-Up	No extractable or relevant data for interventions/outcomes of interest

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526	Stewart	2015	26231697	10.1016/j.jsat.2015.06.002	Effectiveness of Motivational Incentives for Adolescent Marijuana Users in a School-Based Intervention	NRCS (nonpharm, pharmacological interventions N < 100)
527	Strang	2004	15223098	10.1016/j.jsat.2004.05.003	Can the practitioner correctly predict outcome in motivational interviewing?	No extractable or relevant data for interventions/outcomes of interest
528	Suffoletto	2012	22168137	10.1111/j.1530-0277.2011.01646.x	Text-message-based drinking assessments and brief interventions for young adults discharged from the emergency department	Includes transition-aged youth (non-pharmacological interventions)
529	Suffoletto	2013	23552023	10.1186/1745-6215-14-93	Mobile phone text message intervention to reduce binge drinking among young adults: study protocol for a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
530	Suffoletto	2014	25017822	10.1016/j.annemergmed.2014.06.010	A text message alcohol intervention for young adult emergency department patients: a randomized clinical trial	Includes transition-aged youth (non-pharmacological interventions)
531	Suffoletto	2015	26580802	10.1371/journal.pone.0142877	An Interactive Text Message Intervention to Reduce Binge Drinking in Young Adults: a Randomized Controlled Trial with 9-Month Outcomes	Includes transition-aged youth (non-pharmacological interventions)
532	Suffoletto	2016	CN-01401609 (cochrane)		Patterns of Change in Weekend Drinking Cognitions Among Non-Treatment-Seeking Young Adults During Exposure to a 12-Week Text Message Intervention	Includes transition-aged youth (non-pharmacological interventions)
533	Svikis	1997	CN-00144272 (cochrane)		Attendance incentives for outpatient treatment: effects in methadone- and nonmethadone-maintained pregnant drug dependent women	Includes adults (> 25 years)
534	Szapocznik	1986	3722570		Conjoint versus one-person family therapy: further evidence for the effectiveness of conducting family therapy through one person with drug-abusing adolescents	No extractable or relevant data for interventions/outcomes of interest
535	Szapocznik	1988	1989-06560-001 (psychinfo)	10.1037/0022-006X.56.4.552	Engaging adolescent drug abusers and their families in treatment: A strategic structural systems approach	No extractable or relevant data for interventions/outcomes of interest

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536	Szobot	2008	CN-00647808 (cochrane)		A randomized crossover clinical study showing that methylphenidate-SODAS improves attention-deficit/hyperactivity disorder symptoms in adolescents with substance use disorder	RCT, N < 10 per arm
537	Tait	2016	27317044	10.1016/j.drugalcdep.2016.06.005	Emergency department based intervention with adolescent substance users: 10year economic and health outcomes	No extractable or relevant data for interventions/outcomes of interest
538	Tanner-Smith	2018	29706171	10.1016/j.jsat.2018.03.003	Who attends recovery high schools after substance use treatment? A descriptive analysis of school aged youth	Case control/cross sectional
539	Tapert	2003	2003-09555-004 (psychinfo)	10.1300/J029v12n04_04	Depressed mood, gender, and problem drinking in youth	No extractable or relevant data for interventions/outcomes of interest
540	Tetzlaff	2005	16011391	10.1037/0893-164X.19.2.199	Working alliance, treatment satisfaction, and patterns of posttreatment use among adolescent substance users	No extractable or relevant data for interventions/outcomes of interest
541	Thomasius	2005	16097269	10.1024/1422-4917.33.3.217	Familientherapie als Frühintervention bei drogen-abhängigen Jugendlichen, jungen Erwachsenen und deren Müttern--Effektstärken und individuelle Verbesserungsquoten bei den Therapie-Beendern. = Early intervention family therapy in drug-dependent adolescents, young adults, and their mothers--Effect sizes and intraindividual change indices in completers	Single arm (nonpharm, pharmacological interventions N < 200)
542	Thompson	2017	28319159	10.1371/journal.pone.0173272	Drug therapy for alcohol dependence in primary care in the UK: A Clinical Practice Research Datalink study	Includes adults (> 25 years)
543	Thompson	2017	28620272	10.1080/16066359.2016.1193165	Short-term effects of a brief intervention to reduce alcohol use and sexual risk among homeless young adults: Results from a randomized controlled trial	Includes transition-aged youth (non-pharmacological interventions)
544	Thush	2009	19290699	10.1037/a0013789	Influence of motivational interviewing on explicit and implicit alcohol-related cognition and alcohol use in at-risk adolescents	Not all subjects with at least problematic use
545	Timofeev	1999	10467448	10.1142/S0192415X99000185	Effects of acupuncture and an agonist of opiate receptors on heroin dependent patients	No extractable or relevant data for interventions/outcomes of interest

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546	Tingey	2016	2017-07055-013 (psychinfo)	10.5820/aian.2303.2016.248	Entrepreneurship education: A strength-based approach to substance use and suicide prevention for American Indian adolescents	Not all subjects with at least problematic use
547	Tomko	2019	30268706	10.1016/j.addbeh.2018.09.023	Corrigendum to 'The role of depressive symptoms in treatment of adolescent cannabis use disorder with N-Acetylcysteine'	No extractable or relevant data for interventions/outcomes of interest
548	Toumbourou	2013	23968880	10.1016/j.jadohealth.2013.07.005	Reduction of adolescent alcohol use through familyâ€“school intervention: A randomized trial	Not all subjects with at least problematic use
549	Treloar Padovano	2018	29553345		Using Ecological Momentary Assessment to Identify Mechanisms of Change: An Application From a Pharmacotherapy Trial With Adolescent Cannabis Users	No extractable or relevant data for interventions/outcomes of interest
550	Treloar Padovano H	2018	29672090	10.1037/abn0000342	Subjective cannabis effects as part of a developing disorder in adolescents and emerging adults.	Single arm (nonpharm, pharmacological interventions N < 200)
551	Trupin	2011	2011-23745-003 (psychinfo)	10.1080/1067828X.2011.614889	Family integrated transitions: A promising program for juvenile offenders with co-occurring disorders	NRCS (nonpharm, pharmacological interventions N < 100)
552	Tucker	2017	28340904	10.1016/j.jsat.2017.02.008	A group-based motivational interviewing brief intervention to reduce substance use and sexual risk behavior among homeless young adults	Not all subjects with at least problematic use
553	van der Pol	2018	28076983	10.1177/0306624X16687536	Multidimensional Family Therapy Reduces Self-Reported Criminality Among Adolescents With a Cannabis Use Disorder	No extractable or relevant data for interventions/outcomes of interest
554	Van Meter W		2324868	10.1080/02791072.1990.10472202	The case for shorter residential alcohol and other drug abuse treatment adolescents	Single arm (nonpharm, pharmacological interventions N < 200)
555	Vargas-Martínez	2019	31590139	10.1016/j.drugalcdep.2019.107597	Measuring the effects on quality of life and alcohol consumption of a program to reduce binge drinking in Spanish adolescents	Not all subjects with at least problematic use
556	Voogt	2012	22709609	10.1186/1745-6215-13-83	The effectiveness of a web-based brief alcohol intervention in reducing heavy drinking among adolescents aged 15 to 20 years with a low educational background: study protocol for a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest

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557	Voogt	2014	24613632	10.1016/j.drugalcdep.2014.02.009	The effect of the 'What Do You Drink' web-based brief alcohol intervention on self-efficacy to better understand changes in alcohol use over time: randomized controlled trial using ecological momentary assessment	College setting (alcohol interventions)
558	Waldron	2005	16202539	10.1016/j.addbeh.2005.07.001	Profiles of drug use behavior change for adolescents in treatment	No extractable or relevant data for interventions/outcomes of interest
559	Walton	2010	20682932	10.1001/jama.2010.1066	Effects of a brief intervention for reducing violence and alcohol misuse among adolescents: a randomized controlled trial	Not all subjects with at least problematic use
560	Walton	2013	23711998	10.1016/j.drugalcdep.2013.04.020	Computer and therapist based brief interventions among cannabis-using adolescents presenting to primary care: one year outcomes	Not all subjects with at least problematic use
561	Wang	2016	27099500	10.2147/NDT.S105199	A family-oriented therapy program for youths with substance abuse: long-term outcomes related to relapse and academic or social status	NRCS (nonpharm, pharmacological interventions N < 100)
562	Wang		1997-41255-011 (psychinfo)	10.1016/S1001-0742(08)60025-X	An experimental study of drug-given-up in psychotherapy	Includes adults (> 25 years)
563	Warden	2012	22626890	10.1016/j.addbeh.2012.04.011	Predictors of attrition with buprenorphine/naloxone treatment in opioid dependent youth	No extractable or relevant data for interventions/outcomes of interest
564	Watson	2015	27965788	10.1186/s40814-015-0004-4	A randomised controlled feasibility trial of family and social network intervention for young people who misuse alcohol and drugs: study protocol (Y-SBNT)	No extractable or relevant data for interventions/outcomes of interest
565	Watson	2017	28399988	10.3310/hta21150	Youth social behaviour and network therapy (Y-SBNT): adaptation of a family and social network intervention for young people who misuse alcohol and drugs - a randomised controlled feasibility trial	Includes adults (> 25 years)
566	Watt	2006	CN-00613379 (cochrane)	10.1080/09638230600998938	Brief CBT for high anxiety sensitivity decreases drinking problems, relief alcohol outcome expectancies, and conformity drinking motives: evidence from a randomized controlled trial	College setting (alcohol interventions)
567	Watterson	2017	28464810	10.1186/s12889-017-4330-8	Measuring the effectiveness of in-hospital and on-base Prevent Alcohol and Risk-related Trauma in Youth (P.A.R.T.Y.) programs on reducing alcohol related harms in naval trainees: P.A.R.T.Y. Defence study protocol	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
568	Wechsberg	2017	28845096	10.1080/1067828X.2016.1260511	Efficacy of the Young Women's CoOp: An HIV Risk-Reduction Intervention for Substance-Using African-American Female Adolescents in the South	No extractable or relevant data for interventions/outcomes of interest
569	Wechsberg	2018	29996792	10.1186/s12889-018-5665-5	The Young Women's Health CoOp in Cape Town, South Africa: Study protocol for a cluster-randomised trial for adolescent women at risk for HIV	No extractable or relevant data for interventions/outcomes of interest
570	Wegman	2017	27964869	10.1016/S2214-109X(16)30303-5	Relapse to opioid use in opioid-dependent individuals released from compulsory drug detention centres compared with those from voluntary methadone treatment centres in Malaysia: a two-arm, prospective observational study	NRCS (nonpharm, pharmacological interventions N < 100)
571	Weidman	1987	3612889		Family therapy and reductions in treatment dropout in a residential therapeutic community for chemically dependent adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
572	Weiss	2011	21463074	10.1037/a0023031	Interaction effects of age and contingency management treatments in cocaine-dependent outpatients	Includes adults (> 25 years)
573	Weiss	2014	24865619	10.1016/j.jsat.2014.04.003	Substance abuse treatment patients with early onset cocaine use respond as well to contingency management interventions as those with later onset cocaine use	NRCS (nonpharm, pharmacological interventions N < 100)
574	Welsh	2019	31088277	10.1080/02791072.2019.1613585	Treatment Retention and Outcomes with the Adolescent Community Reinforcement Approach in Emerging Adults with Opioid Use	Includes transition-aged youth (non-pharmacological interventions)
575	Wenzel	2019	CN-01960977 (Cochrane)		Youth opioid recovery support intervention: home delivery of extended release naltrexone	No extractable or relevant data for interventions/outcomes of interest
576	Werch	2005	15957680		A brief experimental alcohol beverage-tailored program for adolescents	Not all subjects with at least problematic use
577	Werch	2010	20307126	10.1037/a0017997	A brief image-based prevention intervention for adolescents	Not all subjects with at least problematic use
578	Whicher	2012	2012-06310-006 (psychinfo)	10.1097/ADT.0b013e3182387029	Pilot project to evaluate the effectiveness and acceptability of single-session brief counseling for the prevention of substance misuse in pregnant adolescents	NRCS (nonpharm, pharmacological interventions N < 100)
579	White	2015	25978822		Are there secondary effects on marijuana use from brief alcohol interventions for college students?	College setting (alcohol interventions)

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580	Wilcox	2012	21936751	10.3109/00952990.2011.600393	Compensation effects on clinical trial data collection in opioid-dependent young adults	No extractable or relevant data for interventions/outcomes of interest
581	Wildberger	2019	CN-01961010 (Cochrane)		Relationship between injectable naltrexone and IOP utilization on opioid relapse in youth	No extractable or relevant data for interventions/outcomes of interest
582	Wiljer	2016	27815232	10.2196/resprot.6446	Enhancing Self-Efficacy for Help-Seeking Among Transition-Aged Youth in Postsecondary Settings With Mental Health and/or Substance Use Concerns, Using Crowd-Sourced Online and Mobile Technologies: The Thought Spot Protocol	Not all subjects with at least problematic use
583	Winn	2019	31229188	10.1016/j.jsat.2019.05.009	Enhancing adolescent SBIRT with a peer-delivered intervention: An implementation study	Single arm (nonpharm, pharmacological interventions N < 200)
584	Winters	2000	10829335		The effectiveness of the Minnesota Model approach in the treatment of adolescent drug abusers	NRCS (nonpharm, pharmacological interventions N < 100)
585	Winters	2007	17588490	10.1016/j.jsat.2006.12.003	Long-term outcome of substance-dependent youth following 12-step treatment	NRCS (nonpharm, pharmacological interventions N < 100)
586	Winters		25866459	10.1080/1067828X.2013.777377	Can Parents Provide Brief Intervention Services to Their Drug-Abusing Teenager?	No extractable or relevant data for interventions/outcomes of interest
587	Wintersteen	2005	2005-09654-008 (psychinfo)	10.1037/0735-7028.36.4.400	Do Gender and Racial Differences Between Patient and Therapist Affect Therapeutic Alliance and Treatment Retention in Adolescents?	Single arm (nonpharm, pharmacological interventions N < 200)
588	Wodarski	2010	20799128	10.1080/15433710903176112	Prevention of adolescent reoccurring violence and alcohol abuse: a multiple site evaluation	No extractable or relevant data for interventions/outcomes of interest
589	Wright	2017	28546136	10.2196/resprot.6760	An Ecological Momentary Intervention to Reduce Alcohol Consumption in Young Adults Delivered During Drinking Events: Protocol for a Pilot Randomized Controlled Trial	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
590	Yurasek	2015	26191947	10.1037/pha0000025	A randomized controlled trial of a behavioral economic intervention for alcohol and marijuana use	College setting (alcohol interventions)
591	Zatzick	2014	24733515	10.1001/jamapediatrics.2013.4784	Collaborative care intervention targeting violence risk behaviors, substance use, and posttraumatic stress and depressive symptoms in injured adolescents: a randomized clinical trial	Not all subjects with at least problematic use
592	Zhang	2010	20802847	10.1016/j.jcrimjus.2010.04.012	Delinquency and alcohol-impaired driving among young males: A longitudinal study	Single arm (nonpharm, pharmacological interventions N < 200)
593		2015	NCT01632735 (CT.gov)		Mobile Continuing Care Approach for Youth	Includes transition-aged youth (non-pharmacological interventions)
594		2018	30484743	10.1089/tmj.2018.0201	Feasibility and Acceptability of an Electronic Parenting Skills Intervention for Parents of Alcohol-Using Adolescent Trauma Patients	Not all subjects with at least problematic use
595		2018	30243410	10.1016/j.jsat.2018.08.013	Feasibility, acceptability, and preliminary effects of a brief alcohol intervention for suicidal adolescents in inpatient psychiatric treatment	Not all subjects with at least problematic use
596		2018	29396897	10.1111/add.14179	Four-year follow-up of an internet-based brief intervention for unhealthy alcohol use in young men	Includes adults (> 25 years)
597		2018	30389649	10.2196/11298	Efficacy of an Online Self-Help Treatment for Comorbid Alcohol Misuse and Emotional Problems in Young Adults: Protocol for a Randomized Controlled Trial	No extractable or relevant data for interventions/outcomes of interest
598		2018	30587217	10.1186/s13063-018-3048-y	Treatment effectiveness of a mindfulness-based inpatient group psychotherapy in adolescent substance use disorder - study protocol for a randomized controlled trial	No extractable or relevant data for interventions/outcomes of interest
599		2018	29485676	10.1111/acer.13606	A Randomized Trial of a Personalized Feedback Intervention for Nonstudent Emerging Adult At-Risk Drinkers	Includes transition-aged youth (non-pharmacological interventions)
600		2018	30148142	10.21037/mhealth.2018.07.04	Pilot randomized trial of MOMENT, a motivational counseling-plus-ecological momentary intervention to reduce marijuana use in youth	Includes transition-aged youth (non-pharmacological interventions)

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
601		2018	28865169	10.1111/add.14026	A developmental-based motivational intervention to reduce alcohol and marijuana use among non-treatment-seeking young adults: a randomized controlled trial	Includes transition-aged youth (non-pharmacological interventions)
602		2018	29195590	10.1016/j.jsat.2017.10.012	Age differences in outcomes among patients in the 'Stimulant Abuser Groups to Engage in 12-Step' (STAGE-12) intervention	Includes adults (> 25 years)
603		2018	29505456	10.1097/JAN.0000000000000207	Relational Health and Recovery: Adolescent Girls in Chemical Dependency Treatment	NRCS (nonpharm, pharmacological interventions N < 100)
604		2018	29960918	10.1016/j.drugalcdep.2018.05.020	Marijuana eCHECKUPTO GO: Effects of a personalized feedback plus protective behavioral strategies intervention for heavy marijuana-using college students	Includes transition-aged youth (non-pharmacological interventions)
605		2018	30021712	10.2196/11106	The Family Check-Up Online Program for Parents of Middle School Students: Protocol for a Randomized Controlled Trial	Not all subjects with at least problematic use
606		2018	30030211	10.2196/mhealth.9324	Mobile Phone-Based Ecological Momentary Intervention to Reduce Young Adults' Alcohol Use in the Event: A Three-Armed Randomized Controlled Trial	Includes adults (> 25 years)
607		2018	30126536	10.1016/j.jsat.2018.07.007	Young adults' perceptions of acceptability and effectiveness of a text message-delivered treatment for cannabis use disorder	Includes adults (> 25 years)
608		2018	30359047	10.1037/adb0000413	Feasibility of an interactive voice response system for daily monitoring of illicit opioid use during buprenorphine treatment	Includes adults (> 25 years)
609		2018	30422198	10.1001/jama.2018.12086	Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force	Review
610		2018	30092491	10.1016/j.evalprogplan.2018.07.001	Is culturally based prevention effective? Results from a 3-year tribal substance use prevention program	Not all subjects with at least problematic use
611		2019	30021470	10.1080/09540121.2018.1500008	Adolescent female school dropouts who use drugs and engage in risky sex: effects of a brief pilot intervention in Cape Town, South Africa	No extractable or relevant data for interventions/outcomes of interest
612		2019	30670102	10.1186/s13063-018-3160-z	Effectiveness of a web-based screening and brief intervention with weekly text-message-initiated individualised prompts for reducing risky alcohol use among teenagers: study protocol of a randomised controlled trial within the ProHEAD consortium	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
613		2019	30866967	10.1186/s13012-019-0874-6	Measurement Training and Feedback System for Implementation of family-based services for adolescent substance use: protocol for a cluster randomized trial of two implementation strategies	No extractable or relevant data for interventions/outcomes of interest
614		2019	30782918	10.1136/bmjopen-2018-024776	A trauma-informed substance use and sexual risk reduction intervention for young South African women: a mixed-methods feasibility study	Includes transition-aged youth (non-pharmacological interventions)
615		2019	30940206	10.1186/s13722-019-0141-9	Development of a social media-based intervention targeting tobacco use and heavy episodic drinking in young adults	Includes transition-aged youth (non-pharmacological interventions)
616		2019	30577903	10.1016/j.jsat.2018.11.012	Randomized effectiveness trial of a parent and youth combined intervention on the substance use norms of Latino middle school students	Not all subjects with at least problematic use
617		2019	30640148	10.1016/j.addbeh.2019.01.006	Which behavior change techniques help young adults reduce binge drinking? A pilot randomized clinical trial of 5 text message interventions	Includes adults (> 25 years)
618		2019	135476645 (embase)	10.1080/1067828X.2018.1529645	Brief alcohol interventions for youth in the emergency department: Exploring proximal and distal outcomes	No extractable or relevant data for interventions/outcomes of interest
619			127619233 (embase)		23 - Practical Tools to Support Adolescent Substance Abuse Prevention in Primary Care: A Multi-Site Randomized Controlled Trial of Computer-Facilitated Screening and Provider Brief Advice in the Medical Office	Review
620			CN-01613001 (cochrane)		Effects of topiramate on cannabis use among adolescents and young adults in a randomized controlled clinical trial targeting alcohol misuse	Review
621			CN-01907359 (cochrane)		Implementation and effectiveness of an early intervention program (QuikFix) for young people experiencing alcohol and other drug-related harm	No extractable or relevant data for interventions/outcomes of interest
622			CN-01899196 (cochrane)		Treatment of mindfulness-based psychotherapy in adolescent inpatients with substance use disorders	No extractable or relevant data for interventions/outcomes of interest

No.	Author	Year	PubMed or (Other) ID	DOI	Title	Reason for Exclusion
623			CN-01899372 (cochrane)		Promoting Help-seeking using E-technology for Adolescents (Pro-HEAD). Sub-project 3: web-Based Screening and Brief Intervention for Alcohol Use among Teenagers: added Effects through Extended User Engagement?	No extractable or relevant data for interventions/outcomes of interest
624			CN-01906948 (cochrane)		Prevention of Substance Abuse and Mental Disorders in Children using the Mindfulness- Augmented "Trampoline" Program	No extractable or relevant data for interventions/outcomes of interest
625			NCT02646449 (CT.gov)		Treatment of Young Adults With Comorbid AUD/MDD: A Pilot Medication Trial	RCT, N < 10 per arm

Abbreviations: NRCS = non-randomised controlled study; RCT = randomized controlled trial; nonpharm = study did not evaluate a pharmacological agent

Appendix C. Intervention Coding Manual

Determinations for Each Study

1. Intervention type? (category: Drug; Behav; Drug & Behav)
2. Drugs used (text=drug(s) used in each arm, if applicable)
    2a. Drug note (text=details reported about drug dose, delivery, frequency, etc.)
3. Source (text=additional sources other than primary extracted PMID [e.g., included co-pubs, protocols, cited manuals] used to code intervention content)

Table C-2. Determinations for Each Arm

LABELS

4. SRDR arm name (text=comprised of content labels in order of appearance in extraction sheet)
5. Article arm name (text=specific label for arm as written in article)
6. Is the intervention (as a whole, if includes multiple content components below) well specified? (binary: 0=no; 1=yes)

Code YES if:

Intervention has a specific name that describes the approach

- Primary intervention of interest is guided by a manual or comparable guide to ensure that others could replicate the approach
- The study references treatment fidelity or adherence

Code NO if:

- Intervention is generally not well specified

7. Is the intervention well specified note? (text=specific text describing why intervention is/is not well specified). Consider TIDieR checklist.

INTERVENTION CONTENT

8. Content: Cognitive behavioral (binary: 0=no; 1=yes)

Code YES if:

- Intervention described as focusing on changing the adolescent's thoughts and/or behaviors
- Common brand names may include:
    - Adolescent Community Reinforcement Approach (ACRA)
    - Dialectical Behavior Therapy (DBT)
    - Cognitive Behavioral Therapy (CBT)
    - Cognitive Therapy (CT)

Code NO if:

- No mention of cognitive behavioral therapy

9. Content: Cognitive behavioral note (text=specific labels and/or text to support content label)
10. Content: Motivation building (binary: 0=no; 1=yes)

Code YES if:

- Intervention described as focusing on increasing the adolescent's motivation to change
- Common brand names may include:
    - Motivational Interviewing (MI)
    - Brief Motivational Intervention (BMI)
    - Motivation-Enhancement Therapy (MET)

Code NO if:

- No mention of motivation-building therapy

11. Content: Motivation building note (text=specific labels and/or text to support content label)
12. Content: Educational (binary: 0=no; 1=yes)

Code YES if:

- The intervention is described as psychoeducation, education, or general education
- Common brand names may include:
    - Psychoeducation(al) (PE)
    - Psychoeducation therapy or treatment (PET)
    - Education (ED or EDUC)

Code NO if:

- No mention of psychoeducation or education

13. Content: Educational note (text=specific labels and/or text to support content label)
14. Content: Family focused (binary: 0=no; 1=yes)

Code YES if:

- Common descriptions may include:
    - Family therapy
    - Family-based therapy
    - Family strategic therapy
- Common brand names may include:
    - Brief Strategic Family Therapy (BSFT)
    - Ecological Family Therapy
    - Ecologically Based Family Therapy (EBFT)
    - Educational Family Therapy
    - Family Behavioral Therapy (FBT)
    - Family Functional Therapy/Functional Family Therapy (FFT)
    - Family Systems Therapy (FST)
    - Family Systems Network (FSN)
    - Multidimensional Family Therapy (MDFT)
    - Multi-systemic Therapy (MST)
- The intervention will include BOTH teen and a parent or legal guardian. Do NOT select this category if the intervention targets sibling only or teen + sibling or parents only

Code NO if:

- No mention of family therapy

15. Content: Family focused note (text=specific labels and/or text to support content label)
16. Content: Contingency management (binary: 0=no; 1=yes)

Code YES if:

- Intervention described as using contingency management, motivational incentives, vouchers, or prize draws
- Common brand names may include:
    - Contingency management (CM)
    - Motivational Incentives
    - Voucher-Based Therapy

Code NO if:

- No mention of contingency management

17. Content: Contingency management note (text=specific labels and/or text to support content label)

18. Content: Peer group therapy (binary: 0=no; 1=yes)

Code YES if:

- Intervention described as providing peer group therapy (e.g. nondirective therapy interventions) delivered to

adolescents in a group format

Code NO if:

- No mention of peer group therapy

19. Content: Peer group therapy note (text=specific labels and/or text to support content label)

20. Content: Intensive case management (binary: 0=no; 1=yes)

Code YES if:

- Intervention described as providing support to link adolescents to supportive services (e.g., continuity of care, etc.)

Code NO if:

- No mention of peer group therapy

21. Content: Intensive case management note (text=specific labels and/or text to support content label)

EFFECT MODIFIERS

22. Brief duration (binary 0=no; 1=yes)

Code YES if:

- The intervention content is delivered in <2 sessions

Code NO if:

- The intervention context is delivered > 2 sessions

23. Brief duration note (text=specific description of the duration and frequency of the intervention content above)

24. Delivery group (binary: 0=no; 1=yes)

The goal of the intervention is to address each individual adolescent's substance use, but the delivery mechanism is simultaneous treatment of a group of adolescents

Code YES if:

- The intervention content is described as being delivered in a group format (i.e., delivered to multiple adolescents at the same time
- Any intervention model is fine. Focus on whether the intervention is described as delivered in groups of adolescents

Code NO if:

- No mention of group therapy

25. Delivery group note (text=specific description of the group format)

26. Culturally accommodated intervention (binary: 0=no; 1=yes)

Code YES if:

- The intervention content is described as being culturally sensitive/culturally adapted/specific/tailored

Code NO if:

- No mention of cultural adaptation

27. Culturally accommodated intervention note (text=brief description of how study was culturally sensitive; consider PROGRESS framework)

28. Integrated intervention (binary: 0=no; 1=yes)

Code YES if:

- The intervention content is described targeting substance abuse and a co-occurring disorder

Code NO if:

- No mention of integrated intervention

29. Integrated intervention note (text= specific description of the integrated intervention)
30. General note (text=other information relevant to the intervention not already captured. Note, that this field should not be used to flag studies to be excluded but may be used to flag potential co-publications if not already linked. Also a place to note ordering (e.g., if a study compares MET + CBT vs. CBT + MET)

Appendix D. Baselines

Table D-1. Brief behavioral interventions — baseline data and interventions

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Arnaud, 2015 2016-03749-004 (psychinfo)	1449	alcohol	PU	[16, 18] 16.9 (0.7)	47	outpatient online	online	1. TAU: "Control" 2. MI: "WISEteens"
Arnaud, 2017 27801991	320	alcohol	PU	[nr, 18] 15.7 (1.2)	49	hospital ED	hospital staff	1. TAU: "Treatment as usual" 2. MI (parent): "Brief MI"
Bernstein, 2009 20053238	210	cannabis	PU	[14, 21] nr	63	hospital ED	peer educators	1. TAU: "Assessed control" 2. MI: "Intervention"
Bernstein, 2010 20670329	853	alcohol cannabis	PU	[14, 21] nr	53	hospital ED	peer educators	1. TAU: "Standard assessed control" 2. MI: "Intervention"
Braciszewski, 2018 132804409 (embase)	33	alcohol cannabis other drugs	PU	[18, 19] 18.9 (0.5)	52	exiting foster care	computerized	1. TAU: "Control" 2. MI: "iHeLP"
Brown, 2015 26362000	151	cannabis alcohol	SUD	[13, 17] 15.8 (1)	35	inpatient psychiatric hospital	research staff (Ph.D. psychologists, postdoctoral fellows)	1. TAU: "Treatment as usual" 2. MI: "Motivational interviewing"
Colby, 2018 29750362	167	alcohol	PU	[17, 20] nr	59	community outpatienr	research staff (PhD psychologist, postdoctoral fellow, social worker)	1. TAU: "Attention control" 2. MI: "Brief motivational intervention"
Cunningham, 2015 26347440	836	alcohol cannabis other drugs	PU	[14, 20] 18.6 (1.4)	52	hospital ED	online, therapist (no detail)	1. TAU: "Control" 2. MI: "Computer brief intervention" 3. MI: "Therapist brief intervention"
D'Amico, 2008 18037603	64	alcohol cannabis	PU	[12, 18] 16 (1.8)	48	primary care	therapists (no detail)	1. TAU: "Usual care" 2. MI: "Project CHAT"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
D'Amico, 2018 30138016	294	cannabis alcohol	PU	[12, 18] 15.9 (1.6)	45	outpatient primary care clinic	facilitators	1. TAU: "Usual care" 2. MI: "CHAT intervention"
de Gee, 2014 24969735	171	cannabis	PU	[14, 21] 17.9 (1.8)	76	outpatient community	community clinicians (prevention workers)	1. MI: ""Weed Check" in Dutch" 2. Educ: "Information session"
Dembo, 2014 2014-42452-005 (psychinfo)	180	alcohol cannabis other drugs	PU	[11, 17] 14.8 (1.3)	65	outpatient community (juvenile justice)	therapists (no detail)	1. TAU: "Standard truancy services" 2. MI (parent): "BI-Youth and Parent" 3. MI: "BI-Youth"
Giles, 2019 CN-01953820 (cochrane)	443	alcohol	PU	[14, 15] nr	51	outpatient school	school staff (learning mentors)	1. TAU: "Control" 2. MI: "Brief alcohol intervention"
Marsden, 2006 16771893	342	cannabis alcohol MDMA cocaine	PU	[16, 22] 18.3 (2)	67	community outpatiet	community clinicians, research staff (no detail)	1. TAU: "Control" 2. MI: "Intervention"
Martin, 2008 17869051	40	cannabis alcohol other drugs	PU	[14, 19] 16.5 (1.3)	67	outpatient community	therapists (no detail)	1. TAU: "Delayed treatment condition" 2. MI: "Adolescent Cannabis Check-Up"
Martínez Martínez, 2008 2009-05582-007 (psychinfo)	52	alcohol	PU	[14, 18] 16 (1.5)	65	outpatient school	therapists (no detail)	1. TAU: "Control waitlist" 2. MI: "Experimental"
Mason, 2015 26234955	119	cannabis alcohol	PU	[14, 18] 16.4 (1.2)	29	outpatient research clinic	therapists (no detail)	1. TAU: "Attention control condition" 2. MI: "Peer network counselling"
McCambridge, 2004 14678061	179	cannabis alcohol other drugs	PU	[16, 20] 17.6 (1.1)	55	outpatient school	research staff (PhD psychologist)	1. TAU: "Education-as-usual" 2. MI: "Motivational interviewing"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
McCambridge, 2008 18778385	326	cannabis alcohol other drugs	PU	[16, 19] 18 (1.7)	69	outpatient school	research staff (PhD psychologist, psychology graduates)	1. MI: "Motivational interviewing" 2. Educ: "Drug information and advice-giving"
McCarty, 2019 30883284	148	alcohol cannabis	PU	[13, 18] nr	20	outpatient	school providers	1. TAU: "School-based health clinic visit" 2. MI: "Check Yourself feedback + School-based health visit"
Monti, 1999 10596521	94	alcohol	PU	[18, 19] 18.4 (0.5)	65	hospital ED	research staff (no detail)	1. TAU: "Standard card" 2. MI: "Brief motivational interviewing"
Peterson, 2006 16938063	285	alcohol cannabis amphetamines cocaine heroin	PU	[13, 19] 17.4 (1.5)	55	outpatient community	research staff (Master's level therapists)	1. TAU: "Assessment only" 2. TAU: "Assessment at follow-up only" 3. MI: "Brief motivational enhancement"
Smith, 2015 25551562	48	unspecified	PU	[13, 19] 16.3 (1.4)	77	outpatient community	therapists (no detail)	1. MI: "MI" 2. MI: "MI + normative feedback"
Spijkerman, 2010 21169172	575	alcohol	PU	[15, 20] 18.2 (1.6)	38	outpatient online	online	1. TAU: "Control" 2. MI: "Brief intervention without normative feedback" 3. MI: "Brief intervention with normative feedback"
Spirito, 2004 15343198	152	alcohol	PU	[13, 17] 15.6 (1.2)	64	hospital ED	research staff (Bachelor's level therapists and Master's level therapists)	1. TAU: "Standard care" 2. MI: "Motivational interview"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Spirito, 2011 21383276	125	alcohol	PU	[13, 17] 15.5 (1.2)	48	hospital ED	research staff (Master's level therapists)	1. MI (parent): "Individual Motivational Interview + Family Motivational Interview (Family Check Up)" 2. MI: "Motivational interview"
Spirito, 2017 29252011	69	cannabis alcohol other drugs	PU	[13, 18] 15.8 (1.4)	59	outpatient research clinic (juvenile justice truant court)	research staff (graduate students)	1. MI (parent): "Motivational enhancement therapy + Family Check Up" 2. Educ: "Psychoeducation"
Srisurapanont, 2007 17453612	48	methamphetamine	SUD	[14, 19] 16.9 (1.4)	88	outpatient research clinic	therapists (no detail)	1. MI: "Brief intervention" 2. Educ: "Psychoeducation"
Stein, 2011 21531089	189	cannabis alcohol	PU	[14, 19] nr	nr	residential (juvenile justice)	research staff (no detail)	1. TAU: "Relaxation training" 2. MI: "Motivational interviewing"
Tait, 2004 15194207	249	alcohol cannabis other drugs	PU	[12, 19] 16.7 (1.7)	48	hospital ED	research staff (no detail)	1. TAU: "Standard hospital care" 2. ICM: "Usual hospital care + BI focused on engagement"
Voogt, 2013 CN-01122318 (cochrane)	609	alcohol	PU	[15, 20] 17.3 (1.3)	60	outpatient school	online	1. TAU: "Control" 2. MI: "Experimental"
Walker, 2006 16822119	97	cannabis alcohol other drugs	PU	[14, 19] 15.8 (1.2)	48	outpatient school	research staff (health educators)	1. TAU: "Waitlist control" 2. MI: "Motivational enchancement therapy"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Walker, 2011 21688877	310	cannabis alcohol other drugs	PU	[14, 19] 16 (1.2)	61	outpatient school	health educators (Bachelor's and Master's level therapists)	1. TAU: “Delayed feedback control” 2. MI: “Motivational enhancement therapy” 3. Educ: “Educational feedback control”
Walker, 2016 27762569	252	cannabis alcohol other drugs	PU	[nr, nr] 15.8 (1)	68	outpatient school	research staff (Bachelor's level therapists and Master's level therapists)	1. CBT+MI: “Assessment only check-in” 2. CBT+MI: “Motivational check-in”
Winters, 2007 17563146	79	alcohol cannabis	SUD	[13, 17] 15.6 (nr)	62	outpatient school	therapists (no detail)	1. TAU: “Control” 2. MI: “BI-A” 3. MI: “BI-AP”
Winters, 2012 22000326	315	cannabis alcohol other drugs	PU	[12, 18] nr	nr	outpatient school	therapists (no detail)	1. TAU: “Assessment only control” 2. MI (parent): “Brief Intervention - Adolescent Plus Parent Session” 3. MI: “Brief Intervention - Adolescent Only”

. PMID* = Pubmed identifier if available, otherwise (database name). Abbreviations: N=number randomized; PU = problematic use; SD = standard deviation; ED = emergency department; nr = not reported; CBT = cognitive behavioral therapy; CM = contingency management; Edu = education; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; TAU = treatment as usual; parent = at least one component of the intervention included parent involvement/was targeted towards parents

Table D-2. Nonbrief behavioral interventions — baseline data and interventions

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Amini, 1982 CN-00182281 (cochrane)	87	unspecified	PU	[nr, nr] 16.1 (1)	69	inpatient (experimental) outpatient community (control)	research staff (psychiatry residents, psychology interns)	1. TAU (group): "Inpatient" 2. TAU: "Outpatient"
Azrin, 1994 CN-00241903 (cochrane)	26	cannabis cocaine hallucinogens methamphetamine benzodiazepines	PU	[nr, 18] 16 (nr)	77	outpatient research clinic	research staff (college graduates, graduate students)	1. PeerGroup (group): "Supportive counseling" 2. CBT (parent): "Behavioral program"
Azrin, 2001 2002-13926-001 (psychinfo)	56	alcohol cannabis "hard drugs"	SUD	[12, 17] 15.4 (1.3)	82	outpatient research clinic	research staff (graduate students)	1. Fam[behavioral] (integrated): "Family-behavioral therapy" 2. CBT (integrated): "Individual-cognitive therapy"
Baer, 2007 18072842	117	cannabis alcohol other drug	PU	[13, 19] 17.9 (1.2)	56	outpatient community (drop in center)	therapists (no detail)	1. TAU: "Treatment as usual" 2. MI: "Brief motivational interview"
Burrow-Sanchez, 2012 22866693	35	unspecified	SUD	[13, 18] 15.5 (1.3)	94	outpatient reseach clinic (juvenile justice)	research staff (graduate students)	1. CBT (group, cultural): "Culturally accomodated CBT" 2. CBT (group): "Standard CBT"
Burrow-Sanchez, 2015 25602465	70	alcohol marijuana other drugs	SUD	[13, 18] 15.2 (1.2)	90	outpatient reseach clinic (juvenile justice)	research staff (graduate students)	1. CBT (group, cultural): "Culturally accomodated CBT" 2. CBT (group): "Standard CBT"
D'Amico, 2013 CN-00917707 (cochrane)	193	cannabis alcohol	PU	[14, 18] 16.6 (1.1)	67	outpatient community	community clinicians (control) research staff (graduate students; experimental)	1. PeerGroup (group): "Usual care" 2. MI (group): "Group motivational interviewing (FreeTalk)"
Dakof, 2015 25621927	112	cannabis alcohol other drug	SUD	[13, 18] 16 (1.1)	89	outpatient community (juvenile justice)	community clinicians	1. Fam[ecological]: "Multidimensional family therapy" 2. CBT+MI (group): "Adolescent group therapy"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Dennis, 2004 15501373b	300	cannabis alcohol other drugs	PU	[12, 18] nr	85	outpatient community	community clinicians	1. Fam[ecological] (cultural): "Multidimensional Family Therapy" 2. CBT+MI (group): "Motivational Enhancement Therapy plus Cognitive Behavioral Therapy (MET/CBT) - 5 sessions" 3. CBT (parent): "Adolescent Community Reinforcement Approach"
Dennis, 2004 15501373	213	cannabis alcohol other drugs	PU	[12, 18] nr	84	outpatient community	community clinicians	1. CBT+MI+Educ+ICM (parent, group): "Family education and therapy components (Family Support Network)" 2. CBT+MI (group): "Motivational Enhancement Therapy plus Cognitive Behavioral Therapy (MET/CBT) - 5 sessions" 3. CBT+MI (group): "Motivational Enhancement Therapy plus Cognitive Behavioral Therapy (MET/CBT) - 12 sessions"
Esposito-Smythers, 2011 22004303	80	cannabis alcohol	SUD	[13, 17] 15.7 (1.2)	33	outpatient research clinic	research staff (PhD psychologist, postdoctoral fellow; experimental) community clinicians (control)	1. TAU (integrated): "Enhanced TAU" 2. CBT+MI (parent, integrated): "Integrated CBT"
Figurelli, 1994 7862806	48	alcohol other drugs	PU	[13, 19] nr	62	outpatient community	therapists (substance abuse counselors)	1. TAU: "TAU" 2. CBT: "Cognitively-oriented pre-intervention"
Friedman, 1989 CN-00496580 (cochrane)	169	alcohol cannabis other drugs	PU	[14, 21] 17.9 (1.8)	61	outpatient community	therapists (no detail)	1. Fam[functional]: "Family therapy" 2. CBT (parent, group): "Parent group"
Godley, 2002 12127465	114	alcohol cannabis	SUD	[12, 17] nr	80	outpatient community	case managers	1. TAU: "Usual continuing care" 2. CBT+ICM: "UCC plus an assertive continuing care protocol"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Godley, 2010 20219293	320	cannabis alcohol other drugs	SUD	[12, 18] nr	76	outpatient community	community clinicians	1. TAU (group): "Chestnut's Bloomington Outpatient Treatment" 2. CBT+MI+ICM (group): "Motivational Enhancement Therapy/Cognitive Behavior Therapy-7 session model + Assertive Continuing Care" 3. CBT+MI (group): "Motivational Enhancement Therapy/Cognitive Behavior Therapy-7 session model" 4. CBT+ICM (group): "Chestnut's Bloomington Outpatient Treatment + Assertive Continuing Care"
Godley, 2019 CN-01745749 (cochrane)	402	cannabis alcohol other drugs	SUD	[12, 18] nr	84	residential treatment	volunteers	1. TAU: "Continuing care services as usual" 2. CBT+ICM: "Volunteer recovery support for adolescents"
Henderson, 2016 26992083	126	alcohol other drugs	PU	[12, 17] 15.2 (1.1)	74	outpatient community (juvenile justice)	therapists (no detail)	1. TAU: "Services as usual (SAU)" 2. CBT+ICM: "Adolescent-community reinforcement approach + assertive continuing care"
Henggeler, 1996 8610836	118	alcohol cannabis other drugs	SUD	[12, 17] 15.7 (1)	79	outpatient community	therapists (no detail; experimental); community clinicians (control)	1. TAU (group): "Usual community services" 2. Fam[ecological]: "Home-based multisystemic therapy"
Henggeler, 2006 16551142	161	cannabis alcohol cocaine	SUD	[12, 17] 15.2 (1.1)	83	outpatient community (juvenile justice)	community clinicians	1. PeerGroup (group): "Drug court with community services" 2. PeerGroup (group): "Family court with community services" 3. Fam[ecological]+PeerGroup (group): "Drug court + multisystemic therapy" 4. Fam[ecological]+CM+PeerGroup (group): "Drug court + multisystemic therapy + contingency managment"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Henggeler, 2012 22309470	115	cannabis alcohol other drugs	PU	[12, 17] 15.4 (1)	83	outpatient community (juvenile justice)	community clinicians	1. PeerGroup (group): "Usual services" 2. Fam[ecological]+CM: "Contingency management and family engagement strategies"
Hogue, 2015 25496283	297	alcohol and other drugs	PU	[12, 18] 15.7 (1.5)	52	outpatient community	community clinicians	1. TAU: "Usual care other" 2. Fam[systems/structural]: "Usual care family therapy"
Joanning, 1992 CN-00631575 (cochrane)	134	alcohol cannabis amphetamines barbiturates or hallucinogens	PU	[11, 20] 15.4 (1.9)	nr	outpatient research clinic	research staff (graduate students)	1. PeerGroup (group): "Adolescent group therapy" 2. Fam[systems/structural]: "Family systems therapy" 3. Fam[education] (group): "Family drug education"
Kaminer, 1998 9824170	32	unspecified	SUD	[13, 18] 15.4 (1.5)	62	outpatient research clinic		1. PeerGroup (group): "Interactional group treatment" 2. CBT (group): "Cognitive-behavioral group treatment"
Kaminer, 2002 12436013	88	cannabis alcohol	SUD	[13, 18] 15.4 (1.3)	70	outpatient research clinic	therapist (no detail)	1. Educ (group): "Psychoeducational therapy" 2. CBT (group): "Cognitive behavioral therapy"
Kaminer, 2008 18978635	144	cannabis alcohol	SUD	[13, 18] 15.9 (1.2)	67	outpatient research clinic	therapists (no detail)	1. TAU: "No-active aftercare" 2. CBT+MI: "Brief telephone MI" 3. CBT+MI: "In-person MI"
Kelly, 2017 28742932	59	alcohol and other drugs	SUD	[14, 21] 16.9 (2)	73	outpatient community	therapists (no detail)	1. PeerGroup (group): "Integrated 12-step" 2. CBT+MI (group): "MET/CBT"
Killeen, 2012 22299805	31	cannabis other drugs	SUD	[14, 18] 15.5 (1.2)	84	outpatient community	therapists (no detail)	1. TAU: "Control + community treatment" 2. CM: "Contingency management + community treatment"
Latimer, 2003 12957348	43	cannabis alcohol other drugs	SUD	[14, 17] nr	76	outpatient community	therapists (no detail)	1. Educ (group): "Drugs harm psychoeducation curriculum" 2. CBT+Fam[behavioral] (group): "Integrated family and cognitive-behavioral therapy"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Letourneau, 2017 27629581	107	cannabis alcohol cocaine	PU	[11, 17] 14.9 (0.1)	84	outpatient research clinic (juvenile justice)	research staff (Master's level therapists)	1. TAU (group): "Usual services" 2. CBT+Fam[behavioral]+CM: "Risk reduction therapy for adolescents"
Liddle, 2001 11727882	182	cannabis alcohol and other drugs	PU	[13, 18] 15.9 (1.2)	nr	outpatient community	community clinicians	1. PeerGroup (group): "Adolescent group therapy" 2. Fam[education] (group): "Multifamily educational intervention" 3. Fam[ecological]: "Multidimensional family therapy"
Liddle, 2004 15152709	80	unspecified	PU	[11, 15] 13.7 (1.1)	72	outpatient community	community clinicians	1. Fam[ecological]: "Multidimensional family therapy" 2. CBT (group): "Peer group"
Liddle, 2008 18705691	224	cannabis alcohol other drugs	PU	[12, 17.5] 15.3 (1.2)	18	outpatient community	therapists (Ph.D. psychologists and Master's level therapists)	1. Fam[ecological]: "Multidimensional family therapy" 2. CBT: "Cognitive behavioral therapy"
Liddle, 2018 29866383	113	cannabis alcohol stimulants opioids	SUD	[13, 18] 15.4 (1.1)	75	outpatient community	community clinicians	1. TAU (group): "Residential treatment" 2. Fam[ecological]: "Multidimensional family therapy"
Lowe, 2012 22931079	187	unspecified	PU	[13, 18] 16.4 (1.3)	58	outpatient community (Native American tribal area)	therapist and cultural expert (no detail)	1. PeerGroup (group, cultural): "Cherokee Talking Circle" 2. Educ (group): "Standard Substance Abuse Education"
Najavits, 2006 16858633	33	cannabis alcohol hallucinogens amphetamines cocaine opioids inhalants barbiturates	SUD	[nr, nr] 16.1 (1.2)	0	outpatient research clinic	research staff (PhD psychologists, postdoctoral fellows)	1. TAU (integrated): "Treatment as usual" 2. CBT (integrated): "Seeking Safety psychotherapy"
Ogel, 2011 21609157	62	inhalant cannabis other drugs	SUD	[13, 18] 15.3 (1.4)	nr	inpatient	therapists (no detail)	1. Educ (group): "Control" 2. CBT+Educ (group): "Experimental"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Rigter, 2013 23140805	450	cannabis alcohol	SUD	[13, 18] 16.3 (nr)	85	outpatient community (forensic centers)	community clinicians	1. TAU: "Individual psychotherapy" 2. Fam[ecological]: "Multidimensional family therapy"
Robbins, 2008 18266532	190	cannabis cocaine other drugs	SUD	[12, 17] 15.6 (1.1)	78	outpatient community	research staff (postdoctoral fellow, predoctoral intern, Master's level therapists)	1. TAU: "Community services control" 2. Fam[systems/structural]: "Family process only" 3. Fam[ecological]: "Fully integrated ecosystemic family approach"
Robbins, 2011 21967492	481	cannabis alcohol other drugs	PU	[13, 17] 15.2 (1.2)	78	outpatient community	community clinicians	1. TAU: "Treatment as usual" 2. Fam[systems/structural]: "Brief strategic family therapy"
Rohde, 2014 24491069	170	cannabis alcohol	SUD	[13, 18] 16.2 (1.4)	74	outpatient research clinic	therapists (Master's level therapists; no detail)	1. CBT+Fam[functional] (group, integrated): "FFT followed by CWD" 2. CBT+Fam[functional] (group, integrated): "CWD followed by FFT" 3. CBT+Fam[functional] (group, integrated): "Combining FFT and CWD (Coordinated treatment)"
Rowe, 2016 26879671	154	cannabis alcohol other drug	PU	[13, 17] 15.5 (1.3)	83	Residential (juvenile justice), Outpatient community (juvenile justice)	juvenile detention staff	1. TAU (group, integrated): "Enhanced services as usual" 2. Fam[ecological]: "Multidimensional family therapy"
Santisteban, 2011 21639636	28	cannabis cocaine other drugs	SUD	[14, 17] nr	nr	outpatient community	therapists (no detail)	1. MI+Educ+Fam[systems/structural] (cultural): "Culturally informed and flexible family-based treatment for adolescents (CIFFTA)" 2. Fam[systems/structural]: "Traditional Family Therapy"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Santisteban, 2015 25799306	40	cannabis alcohol cocaine	SUD	[14, 17] nr (16)	1	outpatient community (juvenile justice)	research staff (Ph.D. psychologists; Master's level therapists)	1. TAU: "Individual drug counseling" 2. CBT+Fam[systems/structural] (integrated): "Personality Disorder-Oriented Adolescent Family Therapy (I-BAFT)"
Schaeffer, 2014 23958035	97	cannabis alcohol other drugs	PU	[15, 18] 15.8 (0.9)	83	outpatient community (juvenile justice)	community clinicians	1. TAU: "Community restitution apprentice-focused training" 2. TAU: "Education as usual"
Slesnick, 2005 15878048	124	cannabis alcohol cocaine opiates	PU	[12, 17] 14.9 (1.4)	41	outpatient community	therapists (no detail)	1. TAU: "Service as usual" 2. Fam[ecological]: "Ecologically based family therapy"
Slesnick, 2007 16989957	180	cannabis alcohol other drugs	SUD	[14, 22] 19.2 (2.1)	66	outpatient community (drop in center)	therapists (no detail)	1. TAU: "TAU through the drop in center" 2. CBT: "Community reinforcement approach"
Slesnick, 2009 19522781	119	alcohol cannabis other drugs	PU	[12, 17] 15.1 (1.4)	45	outpatient community	therapists (no detail)	1. TAU: "Service as usual" 2. Fam[functional]: "Office-based functional family therapy" 3. Fam[ecological]: "Home-based ecologically based family therapy"
Slesnick, 2013 23895088	179	unspecified	SUD	[12, 17] 15.4 (1.2)	48	outpatient community (shelter)	community clinicians, research staff (graduate students)	1. MI: "Motivational Interviewing" 2. Fam[ecological]: "Ecologically-Based Family Therapy" 3. CBT: "Community Reinforcement Approach"
Slesnick, 2015 25736623	270	cannabis alcohol other drugs	SUD	[14, 20] 18.7 (1.3)	53	outpatient community (shelter)	therapists (no detail)	1. MI: "Motivational enhancement therapy" 2. ICM: "Case management" 3. CBT: "Community reinforcement approach"
Smith, 2006 17182429	98	cannabis alcohol other drugs	PU	[12, 18] 15.8 (nr)	71	outpatient community	therapists (no detail)	1. Fam[behavioral] (group): "Strengths oriented family therapy" 2. CBT+MI+PeerGroup (group): "The Seven Challenges"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Stanger, 2009 19717250	69	cannabis alcohol	PU	[12, 18] 15.9 (1)	83	outpatient research clinic	research staff (postdoctoral fellows, Master's level therapists)	1. CBT+MI+Fam[behavioral]+CM: "MET/CBT + abstinence CM + family management" 2. CBT+MI+Educ+CM (parent): "MET/CBT + attendance CM + parent psychoeducation"
Stanger, 2015 26004659	153	cannabis alcohol	SUD	[12, 18] 15.8 (1.4)	89	outpatient community	research staff (Master's level therapists)	1. CBT+MI+CM (parent): "MET/CBT+CM+Parent Training" 2. CBT+MI+CM: "MET/CBT+abstinence-based contingency management (CM)" 3. CBT+MI: "Motivational enhancement therapy/cognitive-behavioral therapy (MET/CBT)"
Stanger, 2017 28414474	75	cannabis alcohol	PU	[12, 18] 16.2 (1.2)	75	outpatient research clinic	research staff (postdoctoral fellows)	1. CBT+MI+Fam[behavioral]+CM +ICM: "Experimental" 2. CBT+MI+CM+ICM: "Contriol"
Thush, 2007 16928395	107	alcohol	PU	[14, 18] 15.5 (1)	57	outpatient research clinic	research staff (no detail)	1. TAU: "Information-only control" 2. CBT+MI (group): "Learning to drink"
Tolou-Shams, 2017 CN-01365355 (cochrane)	60	cannabis alcohol other drugs	PU	[12, 18] 15.6 (1.3)	70	outpatient community (juvenile justice family court)	therapists (no detail)	1. Educ: "Adolescent-only health promotion intervention" 2. CBT+Fam[behavioral]: "Family-based affect management"
Trudeau, 2017 2017-00657-001 (psychinfo)	160	alcohol and other drugs	PU	[13, 21] 17.6 (2.1)	43	outpatient onlline	community clinicians	1. TAU: "Attention control" 2. CBT: "Navigating my Journey"
Wagner, 2014 24841864	514	cannabis alcohol other drugs	PU	[14, 18] 16.2 (1.2)	59	outpatient school	therapists (no detail)	1. TAU: "Standard care" 2. CBT+MI: "Guided self-change"
Waldron, 2001 11680557	120	cannabis other drugs	SUD	[13, 17] 15.4 (1)	80	outpatient research clinic	research staff (PhD psychologists, graduate students)	1. Fam[functional]: "FFT" 2. Educ (group): "Group" 3. CBT+MI+Fam[functional]: "Joint" 4. CBT+MI: "CBT"

Author, Year PMID*	N	Substances Used	Severity	Ages [eligible] Mean (sd)	Male %	Setting	Intervention Delivery	Arm Names
Zhang, 2018 30556713	270	alcohol or other drugs	SUD	[14, 20] 18.7 (1.3)	53	Outpatient (drop-in center for homeless youth)	Master's level (counelors, marriage and family therapists or social workers)	1. MI: "Motivational enhancement therapy" 2. ICM: "Case management" 3. CBT: "Community reinforcement approach"

PMID* = Pubmed identifier if available, otherwise (database name). Arm names = Intervention codes, (intervention modifiers) and [family subclassification]: "study arm name". Abbreviations: N=number randomized; SD = standard deviation; ED = emergency department; nr = not reported; CBT = cognitive behavioral therapy; CM = contingency management; Edu = education; Fam = family therapy; ICM = intensive case management; MI = motivational interviewing; TAU = treatment as usual; parent = at least one component of the intervention included parent involvement/was targeted towards parents; Fam = Family therapy; ICM= intensive case management; group = at least one component of the intervention was delivered in a group setting; parent = at least one component of the intervention included parent involvement/was targeted towards parents; integrated = intervention as a whole was designed to treat substance use disorder/problematic use and at least one other diagnoses (e.g., mental health); cultural = intervention designed to meet the unique characteristics of the population in which it was delivered.

-3. Additional baselines

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
nini, 1982 l-00182281 chrane)	United States	single center	nr	RCT	2	52/16/nr	nr	nr	nr	nr	nr	nr	nr	nr
naud, 2015 16-03749-004 ychinfo)	Sweden, Belgium, Czech Republic, Germany	multi-center	Drug Prevention and Information Programme of the European Union	RCT	2	nr/nr/nr	nr	nr	nr	nr	nr	nr	nr	nr
naud, 2017 801991	Germany	multi-center	German Federal Ministry for Education and Research	cluster RCT	2	nr/nr/nr	nr	nr	nr	nr	nr	nr	nr	nr
rin, 1994 l-00241903 chrane)	United States	single center	NIDA	RCT	2	nr/nr/19 (Minority)	nr	96	nr	4	nr	35	nr	8
rin, 2001 02-13926-001 ychinfo)	United States	single center	NIMH	RCT	2	79/2/nr	nr	nr	nr	nr	nr	nr	nr	nr
er, 2007 072842	United States	single center	NIDA	RCT	2	58/8/19 (Multiracial)	nr	nr	nr	nr	nr	nr	nr	nr
rnstein, 2009 053238	United States	single center	NIH, NIDA	RCT	3	4/84/2 (Other)	nr	62	nr	nr	nr	nr	nr	nr
rnstein, 2010 570329	United States	single center	NIAA	RCT	3	26/51/2 (Asian)	nr	nr	nr	nr	nr	nr	nr	nr
aciszewski, 18 2804409 nbase)	United States	single center	NIDA	RCT	2	52/27/21 (Mixed/other)	4	94	nr	nr	nr	nr	nr	nr
own, 2015 362000	United States	multicenter	NIDA	RCT	2	88/6/5 (Other races or more than one race)	73	95	100	18	14	19	6	8

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
rrow-Sanchez, 12 366693	United States	single center	NIDA	RCT	2	nr/nr/nr	nr	nr	100	nr	nr	nr	nr	nr
rrow-Sanchez, 15 602465	United States	single center	NIDA	RCT	2	nr/nr/nr	6	67	100	nr	nr	nr	nr	nr
lby, 2018 750362	United States	single center	NIAA	RCT	2	58/0/1 (Native American)	nr	nr	nr	nr	nr	nr	nr	nr
rnelius, 2009 321268	United States	single center	NIDA, NIAAA	RCT	2	86/8/6 (Mixed race)	100	nr	nr	0	0	0	0	0
rnelius, 2010 576364	United States	single center	NIDA, NIAAA, VA	RCT	2	57/nr/nr	nr	100	nr	0	0	0	0	0
nningham, 15 347440	United States	single center	NIH	RCT	3	79/10/11 (Other)	100	nr	nr	nr	nr	nr	nr	nr
Amico, 2013 -00917707 chrane)	United States	single center	NIDA	RCT	2	45/nr/10 (Mixed and other)	nr	nr	nr	nr	nr	nr	nr	nr
Amico, 2008 037603	United States	single center	NIDA	RCT	2	5/10/nr	nr	nr	nr	nr	nr	nr	nr	nr
kof, 2015 521927	United States	single center	NIDA	RCT	2	nr/33/5 (Other)	26	91	nr	nr	nr	nr	nr	nr
Amico, 2018 138016	United States	multi-center	NIAAA	RCT	2	11/13/8 (Other/multiracial)	94	82	nr	nr	nr	nr	nr	nr
Gee, 2014 969735	Netherland	single center	ZonMW	RCT	2	nr/nr/nr	nr	nr	nr	nr	nr	nr	nr	nr
Sousa, 2008 -00753784 chrane)	India	single center	unclear	RCT	2	nr/nr/nr	100	nr	nr	nr	nr	nr	nr	nr

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
mbo, 2014 14-42452-005 ychinfo)	United States	single center	NIAA	RCT	3	39/23/8 (Other)	nr	nr	nr	nr	nr	nr	nr	nr
nnis, 2004 501373	United States	multicenter	SAMHSA	RCT	3	70/15/9 (Other/mixed)	11	76	1	nr	nr	nr	nr	nr
nnis, 2004 501373b	United States	multicenter	SAMHSA	RCT	3	47/47/5 (Other/mixed)	18	74	1	nr	nr	nr	nr	nr
posito- ythers, 2011 004303	United States	single center	NIAAA	RCT	2	89/3/nr	64	83	nr	nr	nr	nr	nr	nr
urelli, 1994 62806	United States	single center	nr	RCT	2	81/11/nr	nr	nr	100	nr	nr	nr	nr	nr
dling, 2009 298659	United States	single center	American Foundation for Suicide Prevention, the St. Luke's Foundation of Cleveland, Ohio, and by a clinical research grant from Lilly.	RCT	2	73/18/9 (Other)	37	88	nr	nr	nr	nr	nr	nr
edman, 1989 l-00496580 chrane)	United States	single center	NIDA	RCT	2	90/nr/10 (Not white)	88	87	nr	28	14	nr	7	22
ller, 1998 73913	United States	single center	NIDA	RCT	2	nr/nr/nr	7	2	100	nr	nr	nr	1	nr
es, 2019 l-01953820 chrane)	United Kingdom	multi-center	NIHR	RCT	2	91/2/6 (Asian/other)	100	nr	nr	nr	nr	nr	nr	nr
dley, 2002 127465	United States	single center	NIAA	RCT	2	75/18/6 (Other)	59	90	nr	nr	nr	22	nr	nr
dley, 2010 219293	United States	single center	NIDA	RCT	4	75/13/nr	49	76	100	nr	nr	nr	nr	nr

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
dley, 2019 l-01745749 chrane)	United States	nr	NIAAA	RCT	2	49/18/19 (Other/mixed)	nr	nr	95	nr	nr	nr	nr	nr
nzalez, 2015 454835	United States	single center	NIDA	RCT	3	73/nr/nr	0	51	nr	100	nr	nr	nr	nr
ay, 2012 706327	United States	single center	NIDA	RCT	2	83/nr/nr	nr	100	nr	nr	nr	nr	nr	nr
nderson, 2016 992083	United States	single center	CSA/NIDA	RCT	2	79/6/1 (Asian)	nr	nr	100	nr	nr	nr	nr	nr
nggeler, 1996 10836	United States	single center	NIDA	RCT	2	nr/nr/nr	nr	nr	100	nr	nr	nr	nr	nr
nggeler, 2006 551142	United States	single center	NIAA	RCT	4	31/67/2 (Biracial)	nr	nr	100	nr	nr	nr	nr	nr
nggeler, 2012 309470	United States	multicenter	NIDA	RCT	2	57/40/3 (Biracial)	nr	nr	nr	nr	nr	nr	nr	nr
gue, 2015 496283	United States	single center	NIDA	RCT	2	nr/21/6 (Other/mixed)	nr	nr	nr	nr	nr	nr	nr	nr
lbelo, 2017 T00393978 g)	United States	single center	NIDA	RCT	2	nr/nr/nr	nr	100	nr	nr	nr	nr	nr	nr
lbelo, 2017 T00550394 g)	United States	single center	NIAAA	RCT	2	nr/nr/nr	nr	nr	nr	nr	nr	nr	nr	nr
oanning, 1992 l-00631575 chrane)	United States	single center	NIDA	RCT	3	68/2/nr	nr	nr	nr	nr	nr	nr	nr	nr
miner, 1998 24170	United States	single center	nr	RCT	2	nr/nr/nr	nr	nr	100	nr	nr	nr	nr	nr
miner, 2002 436013	United States	single center	NIDA	RCT	2	90/nr/10 (Non white)	nr	nr	100	nr	nr	nr	nr	nr

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
miner, 2008 978635	United States	single center	NIAA	RCT	3	82/4/4 (Biracial/other)	nr	100	nr	nr	nr	nr	nr	nr
lly, 2017 742932	United States	single center	NIAAA	RCT	2	68/11/14 (Mixed)	nr	nr	100	nr	nr	nr	nr	nr
een, 2012 299805	United States	multi-center	NIDA	RCT	2	19/77/3	nr	100	32	nr	nr	nr	nr	nr
timer, 2003 957348	United States	single center	NIDA	RCT	2	81/0/0 (Asian)	nr	nr	100	nr	nr	nr	nr	nr
tourneau, 2017 629581	United States	multicenter	NIDA, NIH	RCT	2	33/30/nr	40	87	23	0	nr	1	nr	nr
dle, 2001 727882	United States	single center	NIDA	RCT	3	51/15/16 (Asian/other)	nr	nr	51	nr	nr	nr	nr	nr
dle, 2004 152709	United States	single center	Substance Abuse and Mental Health Services Administration/Center for Substance Abuse Treatment	RCT	2	3/38/4 (Other)	nr	nr	nr	nr	nr	nr	nr	nr
dle, 2008 705691	United States	single center	NIDA	RCT	2	21/71/nr	26	85	100	nr	nr	nr	nr	nr
dle, 2018 866383	United States	single-center	NIDA	RCT	2	13/18/nr	71	100	33	nr	nr	nr	nr	nr
we, 2012 931079	United States	multi-center	NIDA	RCT	2	0/0/100 (Native American)	nr	nr	nr	nr	nr	nr	nr	nr
rsch, 2005 203961	United States	single center	NIDA	RCT	2	100/0/0	nr	22	100	100	nr	22	nr	nr
rsch, 2016 918564	United States	multicenter	NIDA	RCT	2	81/nr/nr	25	21	nr	100	nr	32	nr	nr
rsden, 2006 771893	UK	multi-center	Department of Health for England and Wales	RCT	2	75/13/14 (Other)	80	90	nr	nr	nr	78	nr	nr

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
rtin, 2008 869051	United States	single center	National Health and Medical Research Council.	RCT	2	nr/nr/nr	nr	85	nr	nr	nr	nr	nr	nr
rtínez rtínez, 2008 09-05582-007 ychinfo)	Mexico	single center	PROMEP (Govt)	RCT	2	nr/nr/nr	100	nr	nr	nr	nr	nr	nr	nr
son, 2015 234955	United States	single center	NIDA	RCT	2	84/nr/16 (White, mixed race, hispanic)	nr	nr	nr	nr	nr	nr	nr	nr
Cambridge, 04 678061	UK	multi-center	NHS	Cluster RCT	2	46/37/20 (Asian/other)	48	76	21	0	nr	23	nr	nr
Cambridge, 08 778385	UK	multi-center	Wellcome Trust	RCT	2	11/52/19 (Asian)	78	100	nr	4	nr	3	nr	8
Carty, 2019 383284	United States	single center	NIAAA	RCT	2	48/9/43 (Asian, hispanic, native American)	100	nr	nr	nr	nr	nr	nr	nr
randa, 2014 489253	United States	single center	NIAA	RCT	2	70/0/10 (Native American)	70	50	nr	nr	nr	nr	nr	nr
randa, 2017 752416	United States	single center	NIDA	RCT	2	50/nr/50 (Minority)	nr	100	nr	nr	nr	nr	nr	nr
nti, 1999 596521	United States	single center	NIAA	RCT	2	79/10/8 (Asian/east indian)	100	nr	nr	nr	nr	nr	nr	nr
javits, 2006 858633	United States	single center	NIAAA	RCT	2	79/3/15 (Asian/pacific islander/multiethnic)	67	79	6	9	6	24	9	24
derhofer, 2003 554608	Austria	single center	unclear	RCT	2	nr/nr/nr	100	nr	nr	nr	nr	nr	nr	nr
derhofer, 2003 385223	Austria	single center	nr	RCT	2	nr/nr/nr	100	0	100	0	0	0	0	0

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
ederhofer, 2003 I-00474316 ochrane)	Austria	single center	unclear	RCT	2	nr/nr/nr	100	nr	nr	nr	nr	nr	nr	nr
Malley, 2015 742208	Unted States	multi-center	NIH	RCT	2	77/8/15 (Various - native American, asian, multiple, and other/refused/unknown.)	100	33	79	0	nr	nr	nr	nr
el, 2011 609157	Turkey	single center	nr	RCT	2	nr/nr/nr	nr	64	nr	nr	nr	nr	nr	nr
terson, 2006 938063	United States	single center	NIAAA	RCT	3	72/3/20 (Native American, asian, other)	87	94	nr	27	10	53	7	36
gs, 2004 187802	United States	single center	NIDA	RCT	2	71/3/0 (Na)	47	69	100	nr	nr	nr	nr	nr
gs, 2007 984403	United States	single center	NIDA	RCT	2	48/14/27	75	88	100	10	8	19	2	18
gs, 2011 871372	United States	multi-center	NIDA	RCT	2	62/23/nr	30	67	0	0	3	9	0	5
ter, 2013 140805	Belgium, France, Germany, The Netherlands, Switzerland	multi-center	(federal) Ministries of Health of Belgium, Germany, The Netherlands, Switzerland, and by MILDT:the Mission Interministerielle de Lutte Contre la Drogue et de Toximanie, France	RCT	2	nr/nr/40 (Foreign descent)	40	100	nr	nr	nr	nr	nr	nr
bbins, 2008 266532	United States	single center	NIDA	RCT	3	0/40/0 (Na)	nr	nr	100	nr	nr	nr	nr	nr
bbins, 2011 967492	United States	multi-center	NIDA	RCT	2	31/22/2 (Other)	26	41	20	nr	nr	nr	nr	nr
hde, 2014 491069	United States	single center	NIDA	RCT	3	61/nr/nr	nr	nr	100	nr	nr	nr	nr	nr
we, 2016 879671	United States	multicenter	NIDA, SAMHSA, CDC, NIAAA, DOJ	RCT	2	nr/61/nr	20	60	8	nr	nr	nr	nr	nr

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
ntisteban, 2011 639636	United States	single center	NIDA, Center for Minority Health and Health Disparities	RCT	2	nr/nr/nr	nr	nr	100	nr	nr	nr	nr	nr
ntisteban, 2015 799306	United States	single center	NIDA	RCT	2	nr/nr/nr	59	79	100	nr	nr	nr	nr	nr
haeffer, 2014 958035	United States	single center	NIDA	RCT	2	18/26/4 (Mixed)	nr	nr	nr	nr	nr	nr	nr	nr
snick, 2005 878048	United States	single center	NIDA	RCT	2	37/7/14 (Native American or other)	11	36	34	10	nr	nr	nr	nr
snick, 2007 989957	United States	single center	nr	RCT	2	41/3/13 (Native American)	70	85	49	nr	nr	nr	nr	nr
snick, 2009 522781	United States	single center	NIAAA/CSAT	RCT	3	29/5/22 (Native American or other)	89	29	17	nr	nr	nr	nr	nr
snick, 2013 895088	United States	single center	NIDA	RCT	3	26/66/7 (Native American, asian, other)	nr	nr	100	nr	nr	nr	nr	nr
snick, 2015 736623	United States	single center	NIDA	RCT	3	20/66/13 (Native American, asian, or other)	nr	78	nr	7	nr	2	nr	nr
ith, 2006 182429	United States	multicenter	SAMHSA	RCT	2	nr/nr/nr	23	49	50	nr	nr	nr	nr	nr
ith, 2015 551562	United States	multicenter	NIAA	RCT	2	23/36/36 (Multiracial)	nr	nr	nr	nr	nr	nr	nr	nr
Sousa, 2014 -01014147 chrane)	India	single center	nr	RCT	2	nr/nr/100 (Indian)	100	nr	nr	nr	nr	nr	nr	nr
ijkerman, 2010 169172	Netherlands	single center	ZonMw	RCT	3	nr/nr/nr	55	nr	nr	nr	nr	nr	nr	nr
irito, 2004 843198	United States	single center	nr	RCT	2	72/7/1 (Asian/east indian)	100	nr	nr	nr	nr	nr	nr	nr
irito, 2011 383276	United States	single center	NIH	RCT	2	71/2/0 (Asian American/ east indian)	100	nr	nr	nr	nr	nr	nr	nr

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
irito, 2017 252011	United States	single center	NIDA	RCT	2	67/19/14 (Multiracial)	nr	nr	nr	nr	nr	nr	nr	nr
surapanont, 07 453612	Thailand	single center	The Office of Narcotics Control Board, Thailand	RCT	2	nr/nr/nr	nr	nr	nr	nr	nr	75	nr	nr
nger, 2009 717250	United States	single center	NIDA, NIAAA, Arkansas Tobacco Settlement fund	RCT	2	91/6/0	nr	nr	nr	nr	nr	nr	nr	nr
nger, 2015 004659	United States	single center	NIH	RCT	3	35/62/3 (Native American, multi-racial)	nr	100	nr	0	0	0	0	0
nger, 2017 414474	United States	single center	NIH	RCT	2	81/nr/19 (Minority)	100	35	nr	nr	nr	nr	nr	nr
ein, 2011 531089	United States	single center	NIDA	RCT	2	nr/nr/nr	nr	nr	nr	nr	nr	nr	nr	nr
t, 2004 194207	Australia	multicenter	Healthway, the West Australian Health Promotion Foundation.	RCT	3	nr/nr/nr	83	nr	nr	nr	nr	nr	nr	nr
urstone, 2010 494267	United States	single center	NIDA, AACAP (Rx from Eli Lilly)	RCT	2	19/9/59 (Other)	nr	nr	nr	nr	nr	nr	nr	nr
ush, 2007 928395	Netherlands	single center	Dutch Health Care Research Organization	RCT	2	nr/nr/nr	100	nr	nr	nr	nr	nr	nr	nr
ou-Shams, 17 l-01365355 chrane)	United States	single center	NIDA	RCT	2	69/10/22 (Asian/other)	78	90	28	nr	nr	nr	nr	nr
deau, 2017 17-00657-001 ychinfo)	United States	single center	NIDA	RCT	2	9/nr/91 (Non-caucasian)	76	nr	74	nr	nr	nr	nr	nr
ogt, 2013 l-01122318 chrane)	Netherlands	multicenter	The Netherlands Organization for Health Research and Development	cluster RCT	2	nr/nr/nr	100	nr	nr	nr	nr	nr	nr	nr

thor, Year MID	Country	Site(s)	Funding Source	Design	# Arms	Percent White\Black\Other(details)	Alcohol (%)	Cannabis (%)	Opioids (%)	NOS (%)	SedHypAnx (%)	Stimulants (%)	Inhalants (%)	Hallucinogens (%)
agner, 2014 841864	United States	multicenter	NIAAA	RCT	2	6/23/14 (Other)	92	nr	90	nr	nr	nr	nr	nr
ldron, 2001 680557	United States	single center	NIDA	RCT	4	38/nr/8 (Native American)	nr	nr	nr	nr	nr	nr	nr	nr
lker, 2006 822119	United States	multicenter	NIDA	RCT	2	53/17/25 (Asian/pacific islander/other)	nr	100	nr	nr	nr	nr	nr	nr
lker, 2011 688877	United States	single center	NIDA	RCT	2	66/10/13 (Multiracial)	nr	100	nr	nr	nr	nr	nr	nr
lker, 2016 762569	United States	single center	NIDA	RCT	2	59/6/35 (Multiracial or asian or other)	nr	100	nr	nr	nr	nr	nr	nr
nters, 2007 563146	United States	single center	NIDA	RCT	2	81/nr/19 (Nonwhite)	nr	nr	100	nr	nr	nr	nr	nr
nters, 2012 000326	United States	single center	NIH	RCT	3	66/nr/34	nr	nr	nr	nr	nr	nr	nr	nr
ody, 2008 984887	United States	multi-center	NIDA	RCT	2	nr/nr/nr	nr	nr	nr	nr	nr	nr	nr	nr
ang, 2018 556713	United States	nr	NIDA	RCT	3	17/68/15	nr	nr	nr	nr	nr	nr	nr	nr

ions: PMID* = Pubmed identifier if available, otherwise (database name); NOS = drug of abuse tot otherwise specified; SedHypAnx = sedatative, hypnotic or anxiolytic; BMBF = German Federal Ministry for Education
CSA = ; CSAT = ; CMHD = Center for Minority Health and Health Disparities; DHCO = Dutch Health Care Research Organization; DPIP=Drug Prevention and Information Programme of the European Union; NHMR
Health and Medical Research Council; NIAA (or NIAAA) = National Institute on Alcohol Abuse and Alcoholism ; NIDA = National Institute on Drug Abuse; NIH = National Institutes of Health ; NIMH = National Instit
ealth; ONCB (Thailand) = The Office of Narcotics Control Board, Thailand ; SAMHSA = Substance Abuse and Mental Health Services Administration; VA = Department of Veteran Affairs ; ZonMw = The Netherlands
ion for Health Research and Development

Appendix E. Outcomes Extracted by Study

Table E-1. Brief interventions

Study, Year PubMed (other database) ID	Heavy Alcohol Use	Use Alcohol	Abstinence Alcohol	Use Cannabis	Abstinence Cannabis	SU Problem Scale	Use AOD	Abstinence AOD	Use Illicit Drugs	Abstinence Illicit Drugs	Use Other Drugs
Arnaud, 2015 2016-03749-004 (psycINFO)	✓	✓	✓	○	○	○	✓	✓	○	○	○
Arnaud, 2017 27801991	✓	○	○	○	○	✓	○	○	○	○	○
Bernstein, 2009 20053238	○	○	○	✓	✓	○	○	○	○	○	○
Bernstein, 2010 20670329	✓	✓	○	○	○	○	○	○	○	○	○
Braciszewski, 2018 132804409 (Embase)	○	○	○	✓	○	○	○	○	○	○	○
Brown, 2015 26362000	○	✓	✓	✓	✓	○	✓	✓	○	○	○
Colby, 2018 29750362	✓	✓	○	○	○	✓	○	○	○	○	○
D'Amico, 2018 30138016	✓	✓	○	✓	○	✓	○	○	○	○	○
de Gee, 2014 24969735	○	○	○	✓	○	✓	○	○	○	○	○
Martin, 2008 17869051	○	○	○	✓	○	✓	○	○	○	○	○
Giles, 2019 CN-01953820 (cochrane)	✓	✓	○	○	○	✓	○	○	○	○	○
Martínez Martínez, 2008 2009-05582-007 (psycINFO)	○	○	✓	○	○	○	○	○	○	○	○
McCambridge, 2004 14678061	○	○	✓	○	✓	○	○	○	○	○	○
McCambridge, 2008 18778385	○	✓	✓	✓	✓	✓	○	○	○	○	○

Study, Year PubMed (other database) ID	Heavy Alcohol Use	Use Alcohol	Abstinence Alcohol	Use Cannabis	Abstinence Cannabis	SU Problem Scale	Use AOD	Abstinence AOD	Use Illicit Drugs	Abstinence Illicit Drugs	Use Other Drugs
McCarty, 2019 30883284	○	✓	○	✓	○	○	○	○	○	○	○
Peterson, 2006 16938063	○	○	○	✓	○	○	○	○	○	○	✓
Spirito, 2004 15343198	✓	✓	○	○	○	○	○	○	○	○	○
Spirito, 2017 29252011	○	○	✓	✓	✓	○	○	○	○	○	○
Stein, 2011 21531089	○	○	○	○	○	✓	○	○	○	○	○
Walker, 2006 16822119	○	○	○	✓	○	○	○	○	○	○	○
Walker, 2011 21688877	○	○	○	✓	○	✓	○	○	○	○	○
Winters, 2007 17563146	✓	✓	○	○	○	✓	○	○	✓	○	○
Winters, 2012 22000326	○	✓	✓	✓	✓	✓	○	○	○	○	○

Abbreviations: ✓ = outcome reported; ○ = outcome not reported; AOD = alcohol and other drugs

Table E-2. Nonbrief interventions

Study, Year PubMed (other database) ID	Heavy Alcohol Use	Use Alcohol	Abstinence Alcohol	Use Cannabis	Abstinence Cannabis	SU Problem Scale	Use AOD	Abstinence AOD	Use Illicit Drugs	Abstinence Illicit Drugs	Use Other Drugs
Azrin, 1994 CN-00241903 (Cochrane)	○	○	○	○	○	○	✓	○	○	○	○

Study, Year PubMed (other database) ID	Heavy Alcohol Use	Use Alcohol	Abstinence Alcohol	Use Cannabis	Abstinence Cannabis	SU Problem Scale	Use AOD	Abstinence AOD	Use Illicit Drugs	Abstinence Illicit Drugs	Use Other Drugs
Azrin, 2001 2002-13926-001 (psycINFO)	○	○	○	○	○	○	○	○	✓	✓	○
Baer, 2007 18072842	○	✓	○	✓	○	○	○	○	○	○	✓
D'Amico, 2013 CN-00917707 (Cochrane)	✓	✓	○	✓	○	✓	○	○	○	○	○
Dakof, 2015 25621927	○	○	○	○	○	○	✓	○	○	○	○
Dennis, 2004 15501373	○	○	○	○	✓	○	○	○	○	○	○
Figurelli, 1994 7862806	○	○	○	○	○	○	○	✓	○	○	○
Godley, 2002 12127465	○	✓	○	✓	○	○	○	○	○	○	○
Godley, 2010 20219293	○	✓	○	○	○	○	✓	○	○	○	○
Henderson, 2016 26992083	○	✓	○	○	○	○	○	✓	○	○	○
Henggeler, 1996 8610836	○	○	○	○	✓	○	○	○	○	○	✓
Henggeler, 2006 16551142	✓	✓	○	✓	○	○	○	○	○	○	✓
Henggeler, 2012 22309470	○	○	○	○	✓	○	○	○	○	○	○
HJoanning, 1992 CN-00631575 (Cochrane)	○	○	○	○	○	○	○	✓	○	○	○
Hogue, 2015 25496283	○	○	○	○	○	○	✓	○	○	○	○
Kaminer, 1998 9824170	○	○	○	○	○	○	✓	○	○	○	○
Kaminer, 2002 12436013	○	○	○	○	○	✓	○	○	○	○	○

Study, Year PubMed (other database) ID	Heavy Alcohol Use	Use Alcohol	Abstinence Alcohol	Use Cannabis	Abstinence Cannabis	SU Problem Scale	Use AOD	Abstinence AOD	Use Illicit Drugs	Abstinence Illicit Drugs	Use Other Drugs
Kaminer, 2008 18978635	✓	✓	✓	○	✓	○	○	○	○	○	○
Kelly, 2017 28742932	○	○	○	○	○	○	○	✓	○	○	○
Latimer, 2003 12957348	○	✓	○	✓	○	○	○	○	○	○	○
Letourneau, 2017 27629581	○	○	○	○	○	○	○	✓	○	○	○
Liddle, 2001 11727882	○	○	○	○	○	○	○	○	✓	○	○
Liddle, 2004 15152709	○	○	○	✓	✓	○	○	○	○	○	○
Liddle, 2008 18705691	○	✓	○	✓	○	○	○	○	○	○	✓
Liddle, 2018 29866383	○	○	○	○	○	○	✓	○	○	○	○
Lowe, 2012 22931079	○	○	○	○	○	✓	○	○	○	○	○
Najavits, 2006 16858633	○	○	○	○	○	✓	○	○	○	○	○
Rigter, 2013 23140805	○	○	○	✓	○	○	○	○	○	○	○
Robbins, 2011 21967492	○	○	○	○	○	○	○	○	✓	✓	○
Santisteban, 2011 21639636	○	○	○	✓	○	✓	○	○	✓	○	○
Slesnick, 2007 16989957	○	○	○	○	○	○	✓	○	○	○	○
Slesnick, 2009 19522781	○	✓	○	○	○	○	○	○	✓	○	○
Slesnick, 2015 25736623	○	✓	○	○	○	○	✓	○	○	○	○

Study, Year PubMed (other database) ID	Heavy Alcohol Use	Use Alcohol	Abstinence Alcohol	Use Cannabis	Abstinence Cannabis	SU Problem Scale	Use AOD	Abstinence AOD	Use Illicit Drugs	Abstinence Illicit Drugs	Use Other Drugs
Smith, 2006 17182429	○	○	○	○	○	○	○	✓	○	○	○
Stanger, 2009 19717250	○	○	○	✓	✓	○	○	○	○	○	○
Stanger, 2015 26004659	○	○	○	✓	✓	○	○	○	○	○	○
Stanger, 2017 28414474	○	✓	✓	✓	✓	○	○	○	○	○	○
Tolou-Shams, 2017 CN-01365355 (Cochrane)	○	✓	○	✓	○	○	○	○	○	○	○
Trudeau, 2017 2017-00657-001 (psycINFO)	○	✓	○	○	○	○	○	○	✓	○	○
Wagner, 2014 24841864	○	✓	○	○	○	○	○	○	✓	○	○
Waldron, 2001 11680557	○	○	○	✓	○	○	○	○	○	○	○
Zhang, 2018 30556713	○	○	○	○	○	○	○	○	✓	○	○

Abbreviations: ✓ = outcome reported; ○ = outcome not reported; AOD = alcohol and other drugs

Appendix F. Brief interventions: Detailed Results

Table F-1. Brief interventions, heavy alcohol use days

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	NMD (95% CI)	SMD (95% CI)	SNMD (95% CI)
27801991	Arnaud, 2017	MI	141 (3 mo)	No	2.69 (2.82)	1.02 (1.51)	-1.67 (-2.1, -1.2)	-0.64 (-1.2, -0.1)	-0.65 (-0.8, -0.5)	-0.25 (-0.5 ,0)
27801991	Arnaud, 2017	TAU	175 (3 mo)	No	2.1 (1.96)	1.07 (1.82)	-1.03 (-1.4, -0.7)		-0.4 (-0.5, -0.3)	
20670329	Bernstein, 2010	MI	202 (3 mo)	No	3.1 (5)	3.9 (3.6)	0.8 (0.1 ,1.5)	-1 (-1.9, -0.1)	0.18 (0 ,0.3)	-0.22 (-0.4 ,0)
20670329	Bernstein, 2010	TAU	197 (3 mo)	No	2.7 (4)	4.5 (3.6)	1.8 (1.2 ,2.4)		0.4 (0.3 ,0.5)	
29750362	Colby, 2018	MI	80 (3 mo)	No	5.63 (4.34)	2.41 (2.99)	-3.22 (-4.2, -2.2)	-1.96 (-3.4, -0.5)	-0.67 (-0.9, -0.5)	-0.41 (-0.7, -0.1)
29750362	Colby, 2018	TAU	81 (3 mo)	No	5.19 (4.18)	3.93 (4.18)	-1.26 (-2.4, -0.2)		-0.26 (-0.5 ,0)	
30138016	D'Amico, 2018	MI	153 (3 mo)	No	0.43 (0.51)	0.92 (1.52)	0.49 (0.3 ,0.7)	-0.07 (-0.4 ,0.3)	0.32 (0.2 ,0.5)	-0.05 (-0.3 ,0.2)
30138016	D'Amico, 2018	TAU	141 (3 mo)	No	0.45 (0.59)	1.01 (1.6)	0.56 (0.3 ,0.8)		0.37 (0.2 ,0.5)	
17563146	Winters, 2007	MI	52 (6 mo)	No	1.89 (0.75)	1.07 (0.68)	-0.82 (-1.1, -0.6)	-0.75 (-1.3, -0.2)	-0.84 (-1.1,-0.6)	-0.77 (-1.3,-0.2)
CN-01953820 (cochrane)	Giles, 2019	MI	178 (12 mo)	No	nr	1.5 (1.7)	0.3 (-0.1, 0.7)			
CN-01953820 (cochrane)	Giles, 2019	TAU	196 (12 mo)	No	nr	1.8 (2.2)				
17563146	Winters, 2007	TAU	26 (6 mo)	No	1.79 (0.93)	1.71 (1)	-0.07 (-0.5 ,0.4)		-0.07 (-0.5 ,0.4)	
2016-03749-004 (psycINFO)	Arnaud, 2015	MI	715 (3 mo)	Yes	1.54 (0.99)	1.39 (0.5)			-0.15 (-0.2,-0.1)	0.01 (-0.1 ,0.1)

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	NMD (95% CI)	SMD (95% CI)	SNMD (95% CI)
2016-03749-004 (psycINFO)	Arnaud, 2015	TAU	734 (3 mo)	Yes	1.58 (1.02)	1.42 (0.47)			-0.16 (-0.2,-0.1)	
15343198	Spirito, 2004	MI	64 (3 mo)	Yes	1.82 (3.46)	1 (2.08)			-0.2 (-0.4 ,0)	-0.07 (-0.4 ,0.3)
15343198	Spirito, 2004	TAU	60 (3 mo)	Yes	2.59 (4.01)	2.06 (3.75)			-0.13 (-0.4 ,0.2)	

Abbreviations: PMID = PubMed ID (or other ID), N=number of subjects;SD = standard deviation;End mean = mean at End;MD = mean difference;NMD = net mean difference;SMD = standardized mean difference; SNMD = standardized net mean difference; MI = motivational interviewing; Educ = psychoeducation; TAU = treatment as usual

Table F-2. Brief interventions, alcohol use days

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	NMD (95% CI)	SMD (95% CI)	SNMD (95% CI)
20670329	Bernstein, 2010	MI	202 (3 mo)	No	6.7 (6.6)	5.5 (4.5)	-1.2 (-2.1 ,-0.3)	-0.8 (-2 ,0.4)	-0.2 (-0.3 ,-0.1)	-0.13 (-0.3 ,0.1)
20670329	Bernstein, 2010	TAU	197 (3 mo)	No	6.1 (6)	5.7 (4.5)	-0.4 (-1.2 ,0.4)		-0.07 (-0.2 ,0.1)	
26362000	Brown, 2015	MI	79 (3 mo)	No	3.7 (5.55)	1.1 (1.72)	-2.6 (-3.8 ,-1.4)	-2.15 (-3.6 ,-0.7)	-0.56 (-0.8 ,-0.3)	-0.46 (-0.8 ,-0.1)
26362000	Brown, 2015	TAU	72 (3 mo)	No	2.35 (3.49)	1.9 (2.71)	-0.45 (-1.3 ,0.4)		-0.1 (-0.3 ,0.1)	
29750362	Colby, 2018	MI	82 (3 mo)	No	9.1 (4.32)	4.3 (3.67)	-4.81 (-5.9 ,-3.7)	-2.64 (-4.4 ,-0.8)	-0.82 (-1 ,-0.6)	-0.45 (-0.8 ,-0.1)
29750362	Colby, 2018	TAU	84 (3 mo)	No	8.02 (5.67)	5.86 (5.38)	-2.17 (-3.6 ,-0.7)		-0.37 (-0.6 ,-0.1)	
30138016	D'Amico, 2018	MI	153 (3 mo)	No	0.86 (0.65)	1.73 (1.86)	0.87 (0.6 ,1.2)	-0.23 (-0.7 ,0.2)	0.47 (0.3 ,0.6)	-0.13 (-0.4 ,0.1)
30138016	D'Amico, 2018	TAU	141 (3 mo)	No	0.78 (0.64)	1.88 (1.95)	1.1 (0.8 ,1.4)		0.6 (0.4 ,0.8)	
18778385	McCambridge, 2008	MI	164 (3 mo)	No	4.4 (5.8)	4 (5.5)	-0.4 (-1.5 ,0.7)	0.3 (-1.27, 1.87)	-0.06 (-0.2 ,0.1)	0.04 (-0.18 ,0.26)
CN-01953820 (cochrane)	Giles, 2019	MI	178 (12 mo)	No	nr		0.27 (-1.4, 1.9)	NA	NA	NA
CN-01953820 (cochrane)	Giles, 2019	TAU	196 (12 mo)	No	nr					
18778385	McCambridge, 2008	Educ	162 (3 mo)	No	4.4 (6.5)	3.7 (5.7)	-0.7 (-1.9 ,0.5)		-0.1 (-0.3 ,0.1)	
30883284	McCarty, 2019	MI	214 (2 mo)	No	2.84 (3.88)	2.66 (4.72)	-0.18 (-0.9 ,0.5)	0.18 (-0.6 ,1)	-0.04 (-0.2 ,0.1)	0.04 (-0.1 ,0.2)
30883284	McCarty, 2019	TAU	214 (2 mo)	No	2.5 (2.78)	2.14 (2.32)	-0.36 (-0.8 ,0.1)		-0.08 (-0.2 ,0)	
22000326	Winters, 2012	MI	256 (6 mo)	No	1.51 (2.25)	1.13 (1.73)	-0.38 (-0.7 ,-0.1)	-2.38 (-3.5 ,-1.3)	-0.14 (-0.2 ,0)	-0.86 (-1.3 ,-0.5)

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	NMD (95% CI)	SMD (95% CI)	SNMD (95% CI)
22000326	Winters, 2012	TAU	55 (6 mo)	No	1.5 (2.23)	3.5 (3.93)	2 (0.9 ,3.1)		0.72 (0.3 ,1.1)	
17563146	Winters, 2007	MI	52 (6 mo)	No	4.46 (0.76)	2.96 (0.76)	-1.5 (-1.8 ,-1.2)	-1.21 (-1.7 ,-0.7)	-1.56 (-1.8 ,-1.3)	-1.27 (-1.8 ,-0.8)
17563146	Winters, 2007	TAU	26 (6 mo)	No	4.36 (0.93)	4.07 (0.79)	-0.29 (-0.7 ,0.1)		-0.3 (-0.7 ,0.1)	
2016-03749-004 (psycINFO)	Arnaud, 2015	MI	715 (3 mo)	Yes	1.98 (0.81)	1.75 (0.47)			-0.24 (-0.3 ,-0.2)	-0.24 (-0.3 ,-0.1)
2016-03749-004 (psycINFO)	Arnaud, 2015	TAU	734 (3 mo)	Yes	1.93 (0.9)	1.93 (0.9)			0 (-0.1 ,0.1)	
15343198	Spirito, 2004	MI	64 (3 mo)	Yes	3.53 (4.67)	2.55 (4.06)			-0.17 (-0.4 ,0.1)	-0.06 (-0.4 ,0.3)
15343198	Spirito, 2004	TAU	60 (3 mo)	Yes	4.18 (4.97)	3.54 (5.39)			-0.11 (-0.4 ,0.2)	

Abbreviations: PMID = PubMed ID (or other ID), N=number subjects;SD = standard deviation;End mean = mean at End;MD = mean difference;NMD = net mean difference;SMD = standardized mean difference; SNMD = standardized net mean difference; MI = motivational interviewing; Educ = psychoeducation; TAU = treatment as usual; NA = not applicable

Table F-3. Brief interventions, alcohol abstinence

PMID	Citation	Intervention	x	N	Log OR (95% CI)	OR (95% CI)
2016-03749-004 (psycINFO)	Arnaud, 2015	MI	491	715	0.24 (95% CI: 0.03 , 0.46)	1.28 (95% CI: 1.03 , 1.59)
2016-03749-004 (psycINFO)	Arnaud, 2015	TAU	464	734		
26362000	Brown, 2015	MI	23	69	-0.52 (95% CI: -1.21 , 0.17)	0.59 (95% CI: 0.3 , 1.18)
26362000	Brown, 2015	TAU	32	70		
2009-05582-007 (psycINFO)	Martínez Martínez, 2008	MI	8	23	2.95 (95% CI: 0.02, 5.89)	19.19 (95% CI: 1.02, 360.51)

PMID	Citation	Intervention	x	N	Log OR (95% CI)	OR (95% CI)
2009-05582-007 (psycINFO)	Martínez Martínez, 2008	TAU	0	17		
14678061	McCambridge, 2004	MI	7	86	1.74 (95% CI: -0.39, 3.86)	5.67 (95% CI: 0.68, 47.29)
14678061	McCambridge, 2004	TAU	1	65		
18778385	McCambridge, 2008	MI	71	164	0.26 (95% CI: -0.18, 0.7)	1.3 (95% CI: 0.83, 2.02)
18778385	McCambridge, 2008	Educ	60	162		
29252011	Spirito, 2017	MI	11	32	0.19 (95% CI: -0.85, 1.23)	1.2 (95% CI: 0.43, 3.41)
29252011	Spirito, 2017	Educ	10	33		
22000326	Winters, 2012	MI	130	256	1.04 (95% CI: 0.4, 1.68)	2.82 (95% CI: 1.49, 5.35)
22000326	Winters, 2012	TAU	15	56		
22000326	Winters, 2012	TAU	15	56		

Abbreviations: PMID = PubMed ID (or other ID), N=number of subjects; x=number abstinent; N=number of subjects; Log OR=log(odds ratio); OR=odds ratio; 95%CI=95% confidence interval ; MI = motivational interviewing; Educ = psychoeducation; TAU = treatment as usual

Table F-4. Brief interventions, cannabis use days

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	NMD (95% CI)	SMD (95% CI)	SNMD (95% CI)
20053238	Bernstein, 2009	MI	41 (3 mo)	No	19 (10.9)	14.2 (10.8)	-4.8 (-8.5 ,-1.1)	-3.2 (-8.1, 1.7)	-0.4 (-0.7, -0.1)	-0.27 (-0.7, 0.1)
20053238	Bernstein, 2009	TAU	54 (3 mo)	No	15.3 (10.1)	13.7 (11.1)	-1.6 (-4.9 ,1.7)		-0.13 (-0.4, 0.1)	
132804409 (embase)	Braciszewski, 2018	MI	12 (3 mo)	No	19.79 (12)	14.09 (11.83)	-5.69 (-13.6 ,2.3)	-2.22 (-12.3, 7.9)	-0.43 (-1, 0.2)	-0.17 (-0.9, 0.6)
132804409 (embase)	Braciszewski, 2018	TAU	18 (3 mo)	No	22.1 (10.61)	18.63 (11.78)	-3.47 (-9.8 ,2.8)		-0.26 (-0.7, 0.2)	

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	NMD (95% CI)	SMD (95% CI)	SNMD (95% CI)
26362000	Brown, 2015	MI	79 (3 mo)	No	14.9 (10.1)	9 (8.91)	-5.9 (-8.5 ,-3.3)	-0.5 (-4.3, 3.3)	-0.5 (-0.7, -0.3)	-0.04 (-0.4, 0.3)
26362000	Brown, 2015	TAU	72 (3 mo)	No	14.6 (10.8)	9.2 (9.05)	-5.4 (-8.2 ,-2.6)		-0.46 (-0.7, -0.2)	
30138016	D'Amico, 2018	MI	153 (3 mo)	No	0.82 (0.7)	2.13 (2.68)	1.3 (0.9 ,1.7)	0.1 (-0.5, 0.7)	0.52 (0.4, 0.7)	0.04 (-0.2, 0.3)
30138016	D'Amico, 2018	TAU	141 (3 mo)	No	0.78 (0.68)	1.98 (2.53)	1.2 (0.8 ,1.6)		0.48 (0.3, 0.6)	
24969735	de Gee, 2014	MI	45 (3 mo)	No	19.71 (9.43)	18.86 (9.86)	-0.86 (-4.1 ,2.4)	0 (-10.8 ,10.8)	-0.07 (-0.4, 0.2)	0 (-0.1, 0.1
24969735	de Gee, 2014	Educ	53 (3 mo)	No	18.43 (9.43)	17.57 (10.71)	-0.86 (-4.1 ,2.4)		-0.07 (-0.4, 0.2)	
17869051	Martin, 2008	MI	20 (3 mo)	No	24.7 (8.2)	18.1 (12.03)	-6.6 (-12.2 ,-1)	-6.3 (-14.2, 1.6)	-0.53 (-1, -0.1)	-0.5 (-1.1, 0.1)
17869051	Martin, 2008	TAU	20 (3 mo)	No	18.47 (10.47)	18.17 (10.53)	-0.3 (-5.9 ,5.3)		-0.02 (-0.5, 0.4)	
18778385	McCambridge, 2008	MI	164 (3 mo)	No	17.3 (9.8)	14.6 (11.7)	-2.7 (-4.7 ,-0.7)	-0.3 (-4.6 ,4)	-0.2 (-0.4, -0.1)	-0.02 (0, 0))
18778385	McCambridge, 2008	Educ	162 (3 mo)	No	18.3 (10.4)	15.9 (11.6)	-2.4 (-4.5 ,-0.3)		-0.18 (-0.3, 0)	
30883284	McCarty, 2019	MI	214 (2 mo)	No	4.78 (8.12)	3.92 (7.54)	-0.86 (-2.1 ,0.4)	0.81 (-1, 2.7)	-0.09 (-0.2, 0)	0.08 (-0.1, 0.3)
30883284	McCarty, 2019	TAU	214 (2 mo)	No	5.47 (9.15)	3.8 (6.72)	-1.67 (-3 ,-0.3)		-0.17 (-0.3, 0)	
16938063	Peterson, 2006	MI	69 (3 mo)	No	15.77 (11.05)	11.83 (11.74)	-3.94 (-7.2 ,-0.6)	0.5 (-4.1, 5.1)	-0.28 (-0.5, 0)	0.04 (-0.3, 0.4)
16938063	Peterson, 2006	TAU	77 (3 mo)	No	16.58 (11.83)	12.14 (12.08)	-4.44 (-7.7 ,-1.2)		-0.31 (-0.5, -0.1)	
29252011	Spirito, 2017	MI	32 (3 mo)	No	11.67 (9.67)	9 (11.67)	-2.67 (-7.2 ,1.8)	0 (-22.5 ,22.5))	-0.2 (-0.5, 0.1)	0 (-0.1, 0.1)
29252011	Spirito, 2017	Educ	33 (3 mo)	No	16.33 (11.67)	13.67 (12)	-2.67 (-7.5 ,2.2)		-0.2 (-0.6, 0.2)	

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	NMD (95% CI)	SMD (95% CI)	SNMD (95% CI)
21688877	Walker, 2011	MI	101 (3 mo)	No	19.74 (6.71)	15.9 (9.84)	-3.84 (-5.9 ,-1.8)	-3.48 (-6.3, -0.6)	-0.37 (-0.6, -0.2)	-0.33 (-0.6, -0.1)
21688877	Walker, 2011	Educ	100 (3 mo)	No	19.74 (7.22)	17.27 (9.89)	-2.47 (-4.6 ,-0.4)	-1.37 (-5.7 ,3)	-0.24 (-0.4, 0)	-0.13 (-0.2, -0.1)
21688877	Walker, 2011	TAU	104 (3 mo)	No	19.09 (7.28)	18.73 (9.49)	-0.36 (-2.4 ,1.6)		-0.03 (-0.2, 0.2)	
16822119	Walker, 2006	MI	47 (3 mo)	No	19.85 (8.51)	15.53 (11.64)	-4.33 (-7.9 ,-0.7)	-2.29 (-7.1, 2.5)	-0.36 (-0.7, -0.1)	-0.19 (-0.6, 0.2)
16822119	Walker, 2006	TAU	50 (3 mo)	No	18.41 (8.47)	16.38 (10.3)	-2.03 (-5.2 ,1.2)		-0.17 (-0.4, 0.1)	
22000326	Winters, 2012	MI	256 (6 mo)	No	7.94 (10.34)	3.36 (5.41)	-4.59 (-5.9 ,-3.3)	0.58 (-1.7, 2.9)	-0.46 (-0.6, -0.3)	0.06 (-0.2, 0.3)
22000326	Winters, 2012	TAU	55 (6 mo)	No	10.13 (6.03)	4.97 (6.03)	-5.17 (-7.1 ,-3.2)		-0.52 (-0.7, -0.3)	

Abbreviations: PMID = PubMed ID (or other ID), N=number randomized;SD = standard deviation;End mean = mean at End;MD = mean difference;NMD = net mean difference;SMD = standardized mean difference; SNMD = standardized net mean difference; MI = motivational interviewing; Educ = psychoeducation; TAU = treatment as usual

Table F-5. Brief interventions, cannabis abstinence

PMID	Citation	Intervention	x	N	Log OR (95% CI)	OR (95% CI)
20053238	Bernstein, 2009	MI	6	42	0.13 (95% CI: -1.04, 1.31)	1.14 (95% CI: 0.35, 3.69)
20053238	Bernstein, 2009	TAU	7	55		
26362000	Brown, 2015	MI	16	69	-0.55 (95% CI: -1.29, 0.2)	0.58 (95% CI: 0.27, 1.22)
26362000	Brown, 2015	TAU	24	70		
14678061	McCambridge, 2004	MI	16	97	1.35 (95% CI: 0.21, 2.49)	3.85 (95% CI: 1.23, 12.03)
14678061	McCambridge, 2004	TAU	4	82		

PMID	Citation	Intervention	x	N	Log OR (95% CI)	OR (95% CI)
18778385	McCambridge, 2008	MI	35	164	0.35 (95% CI: -0.21, 0.91)	1.42 (95% CI: 0.81, 2.49)
18778385	McCambridge, 2008	Educ	26	162		
29252011	Spirito, 2017	MI	10	32	1.51 (95% CI: 0.11, 2.92)	4.55 (95% CI: 1.12, 18.48)
29252011	Spirito, 2017	Educ	3	33		
22000326	Winters, 2012	MI	145	257	0.77 (95% CI: 0.17, 1.36)	2.16 (95% CI: 1.19, 3.91)
22000326	Winters, 2012	TAU	21	56		

Abbreviations: PMID = PubMed ID (or other database ID), N=number of subjects; x=number abstinent; N=number of subjects; Log OR=log(odds ratio); OR=odds ratio; 95%CI=95% confidence interval; MI = motivational interviewing; Educ = psychoeducation; TAU = treatment as usual

Table F-6. Brief interventions, substance use problem scales reported

Score Name	Description	Item Number	Score Range	Score Direction	Score Source
Brief Young Adult Alcohol Consequences Questionnaire (BYAACQ)	This scale can help assess alcohol problems among college students, track changes in alcohol problems throughout college, and measure the response to alcohol interventions. It consists of 24-items and was derived from the 48-item Young Adult Alcohol Consequences Questionnaire. The B-YAACQ has items that tap the full range of the alcohol problems continuum from signs of excessive drinking to symptoms consistent with alcohol abuse and alcohol dependence.	24	0-24	higher score, greater problems	Kahler CW, Strong DR, Read JP (2005) Toward efficient and comprehensive measurement of the alcohol problems continuum in college students: the Brief Young Adult Alcohol Consequences Questionnaire. Alcohol Clin Exp Res 29:1180–1189.
Cannabis Problems Identification Test (CUPIT (subscale problems))	The CUPIT is a self-report questionnaire with two subscales (Bashford et al., 2010). Ten items reflect impaired control over cannabis use (subscale Impaired Control) with scores ranging between 0 and 58. An example of an item from the Impaired Control subscale is: "Over the last 3 months, how often have you used cannabis first thing in the morning?", with the following response options: "never, once or twice, less than monthly, monthly, one day a week, several days a week or daily/always". Six items reflect adverse consequences of cannabis use (subscale Problems) with scores ranging between 0 and 24. An example of an item from the Problems subscale is: "Over the last 3 months, did your use of cannabis ever interfere with (get in the way of) your work at school, your job, or your home life?", with the following response options: 'never, sometimes, quite often, very often and always/all the time'.	6	0-24	higher score, greater problems	Bashford, J., Flett, R., & Copeland, J. (2010). The Cannabis Use Problems Identification Test (CUPIT): Development, reliability, concurrent and predictive validity among adolescents and adults. Addiction, 105, 615–625.
Cannabis Problems Questionnaire (CPQ)		22	0-22		Copeland J, Gilmour S, Gates P, Swift W. The Cannabis Problems Questionnaire: factor structure, reliability, and validity. Drug Alcohol Depend [Internet] 2005;80(3):313–9. Available from: http://dx.doi.org/10.1016/j.drugalcdep.2005.04.009
DSM-IV, alcohol (DSM-IV, alcohol)	Two sets of questions based on DSM-IV criteria addressed whether adolescents had experienced consequences due to alcohol or marijuana use (Tucker et al., 2003). There were six items for alcohol (e.g., missed school or work, passed out) and five for marijuana (e.g., got into trouble at school or home, had difficulty concentrating). Both scales average responses across items that are rated on a four-point scale (never, one time, two times, three or more times) and are reliable with adolescents (α = .77 for marijuana and α = .81 for alcohol).	6	4-point scale	higher score, greater problems	Tucker, J. S., Orlando, M., & Ellickson, P. L. (2003). Patterns and correlates of binge drinking trajectories from early adolescence to young adulthood. Health Psychology, 22, 79−87.

Score Name	Description	Item Number	Score Range	Score Direction	Score Source
Global Assessment of Individual Needs - Quick (GAIN-Q (SPS))				higher score, greater problems	Dennis, M.; Scott, C.; Godley, M.; Funk, R. Comparisons of Adolescents and Adults by ASAM Profile Using GAIN Data from the Drug Outcome Monitoring Study (DOMS): Preliminary Data Tables. Bloomington, IL, Chestnut Health Systems; 1999.
Marijuana Problem Inventory (MPI)	The Marijuana Problems Index (Johnson & White, 1995) is a 23-item measure adapted from the Rutgers Alcohol Problem Index (White & LaBouvie, 1989) that assesses for a variety of marijuana-related negative consequences. The MPI assesses the frequency of problems on a rating scale of 0 (never) to 4 (more than 10 times) as a result of marijuana use. The total MPI score for each participant was computed by adding the 23 item scores. Alpha reliability coefficients at baseline and follow-ups ranged from .86–.97.	23	0-92	higher score, greater problems	V. Johnson, H.R. White. An investigation of factors related to intoxicated driving behaviors among youth Journal of Studies on Alcohol, 50 (4) (1989), pp. 320-330
Marijuana Problem Inventory (MPI)	The Marijuana Problems Index (Johnson & White, 1995) is a 23-item measure adapted from the Rutgers Alcohol Problem Index (White & LaBouvie, 1989) that assesses for a variety of marijuana-related negative consequences. The MPI assesses the frequency of problems on a rating scale of 0 (never) to 4 (more than 10 times) as a result of marijuana use. The total MPI score for each participant was computed by adding the 23 item scores. Alpha reliability coefficients at baseline and follow-ups ranged from .86–.97.	23	0-92	higher score, greater problems	Johnson V, White HR. The relationship between work-specific and generalized stress and alcohol and marijuana use among recent entrants to the labor force. Journal of Drug Issues. 1995; 25(2):237–251.
Personal Consequences Scale (PEI-PCS)	This 11-item self-report scale from the Personal Experience Inventory (Henly & Winters, 1988) focuses on negative consequences of alcohol use and other drug involvement, including legal, health, motor vehicle, social, and family (.92; test–retest .87). Each item has a 4-point response option (strongly disagree, disagree, agree, strongly agree); scores range from 11 to 44. The PCS was administered at intake and the 6-months follow-up.	11	11-44	higher score, greater problems	Henly, G. A., & Winters, K. C. (1988). Development of problem severity scales for the assessment of adolescent alcohol and drug abuse. International Journal of the Addictions, 23, 65–85.
Personal Experience Inventory items (PEI-PCS)	This 11-item self-report scale from the Personal Experience Inventory (Henly & Winters, 1988) focuses on negative consequences of alcohol and other drug involvement, including legal, health, motor vehicle, social, and family (α = .92, test–retest = .87). Each item has a 4-point response option (strongly disagree, disagree, agree, and strongly agree); score range is 11–44.	11	11-44	higher score, greater problems	Henly, G. A., & Winters, K. C. (1988). Development of problem severity scales for the assessment of adolescent alcohol and drug abuse. International Journal of the Addictions, 23, 65–85.

Score Name	Description	Item Number	Score Range	Score Direction	Score Source
Personal Experiences Inventory (PEI (subscale))	PEI has two sections: chemical involvement problem (153 items) and psychosocial problems (147 items), each with multiple subscales (see Results). Scaling varies based on the section, including frequencies and Likert ratings (e.g., Bstrongly agree^). Psychometric information is in the PEI manual. Manual description: PEI is a 276-items self-report Questionnaire made to identify problems commonly associated with adolescent substance abuse. PEI is designed to document the onset, nature and degree of alcohol and other substance involvement, and to identify the personal risk factors that may precipitate or maintain substance abuse. Subscales: Substance use problem severity (10 scales: 94 items). Substance use frequency/onset: 19 items. Personal risk factors (8 scales: 79 items). Environmental risk factors (4 scales: 35 items). Problem screens such as school problems, family problems, and psychiatric disorders (6 screens: 31 items). Validity indices (5 scales: 70 items).	147	NR	higher score, greater problems	Winters KC, Henly GA. Personal Experience Inventory Test and Manual. Los Angeles: Western Psychological Services; 1989.
Revised Behavior Problems Checklist subscales' composite (RBPC subscales)	The Revised Behavior Problems Checklist (Quay & Peterson, 1987) Conduct Disorder and Socialized Aggression subscales were used to create a composite score of parent reported adolescent behavior problems. Internal consistency reliability was high at baseline and follow-up (αs > .90).	39	NR	higher score, greater problems	Quay, HC.; Peterson, DR. Manual for the Revised Behavioral Problem Checklist. Department of Psychology, University of Miami; Coral Gables, FL: 1987.
Risks and Consequences Questionnaire (RCQ-M)	The Risks and Consequences Questionnaire (RCQ) measures problems associated with alcohol and marijuana use (missing school, relationship difficulty, etc.). At baseline it covers 12 months pre-incarceration and at 3 months after release it covers 90 days post-incarceration. Alcohol (RCQ-A) and marijuana (RCQ-M) scales (11 items, each) are scored according to whether events occurred (yes/no). It is reliable and valid for use with incarcerated adolescents, with Cronbach alpha ranging from 0.72 to 0.83 (Stein et al., 2010a).	11	NR	higher score, greater problems	Stein, L.A.R., Lebeau, R., Clair, M., Rossi, J.S., Martin, R.M., Golembeske, C., 2010a. Validation of a measure to assess alcohol- and marijuana-related risks and consequences among incarcerated adolescents. Drug Alcohol Depend. 109, 104–113.
Rutgers Alcohol Problem Index (RAPI)	The original RAPI is a 23-item self-administered screening tool for assessing adolescent problem drinking. It was developed in order to create a conceptually sound, unidimensional, relatively brief, and easily administered instrument to assess problem drinking in adolescence.	23	0-92	higher score, greater problems	Towards the assessment of adolescent problem drinking. White HR, Labouvie EW. J Stud Alcohol. 1989 Jan; 50(1):30-7

Score Name	Description	Item Number	Score Range	Score Direction	Score Source
Rutgers Alcohol Problems Index / Severity of Dependence Scale (RAPI/SDS)	The number of cannabis related consequences (CC) in the past 3 months consisted of 23 items from the adapted version (Vandrey et al., 2005) of the Rutgers Alcohol Problems Index (White and Labouvie, 1989) and 5-items from the Severity of Dependence Scale (Martin et al., 2006): interpersonal (e.g., had a fight, argument or bad feelings with a friend), intrapersonal (e.g., missed out on other things because you spent too much money on cannabis), and substance use disorder symptoms (e.g., kept smoking when you promised yourself not to) (= 0.95).	28	NR	higher score, greater problems	Vandrey, R., Budney, A.J., Kamon, J.L., Stanger, C., 2005. Cannabis withdrawal in adolescent treatment seekers. Drug Alcohol Depend. 78, 205–210. / Martin, G., Copeland, J., Gates, P., Gilmour, S., 2006. The Severity of Dependence Scale (SDS) in an adolescent population of cannabis users: reliability, validity and diagnostic cut-off. Drug Alcohol Depend. 83, 90–93.
Severity of Dependence Scale (SDS)	Severity of dependence for heroin, cocaine and amphetamine was measured by a Severity of Dependence Scale (SDS). The total SDS score was derived from five items, each of which was scored on a four-point scale (scored 0-3). Since severity of dependence can be expected to vary over time, the SDS measures were requested for recent drug use. The five items related to problems of dependence experienced at any time in the last year and all items were completed separately for heroin, cocaine and amphetamine. The items were: (1) Did you think that your use of [named drug] was out of control? (2) Did the prospect of missing a fix (or dose) or not chasing make you anxious or worried? (3) Did you worry about your use of [named drug]? (4) Did you wish you could stop? (5) How difficult did you find it to stop or go without [named drug]?	5	0-15	higher score, greater problems	Gossop, M., Griffiths, P., Powis, B., & Strang, J. (1992). Severity of dependence and route of administration in heroin, cocaine and amphetamines. British Journal of Addiction, 87, 1527−1536.
Teen Addiction Severity Index (T-ASI)	The Teen Addiction Severity Index (T-ASI) is a semistructured interview (Kaminer et al., 1991) modified from the Addiction Severity Index (McLellan et al., 1980) to fill the need for a reliable, valid, and standardized instrument for evaluating the severity of adolescent substance abuse and associated problem domains. The T-ASI was found to have good psychometric properties (Kaminer et al., 1993). The T-ASI problem domains include alcohol, substance use, school or mployment, family, peer/social, legal, and psychiatric. Each domain is scored as the mean of three scales (range: 0 to 4): a) youth's perception of the importance of the problem; b) youth's perception of the need for treatment for the problem; and c) rater's perception of the seriousness of the problem. The T-ASI also assesses the number of substances used, recency in controlled environment, age of first alcohol use, and age of first substance use.	NR	NR	higher score, greater problems	Kaminer Y, Bukstein OG, Tarter TE (1991) The Teen Addiction Severity Index: Rationale and reliability. Int J Addict 26:219–226.

Score Name	Description	Item Number	Score Range	Score Direction	Score Source
Brief Young Adult Alcohol Consequences Questionnaire (BYAACQ)	This scale can help assess alcohol problems among college students, track changes in alcohol problems throughout college, and measure the response to alcohol interventions. It consists of 24-items and was derived from the 48-item Young Adult Alcohol Consequences Questionnaire. The B-YAACQ has items that tap the full range of the alcohol problems continuum from signs of excessive drinking to symptoms consistent with alcohol abuse and alcohol dependence.	24	0-24	higher score, greater problems	Kahler CW, Strong DR, Read JP (2005) Toward efficient and comprehensive measurement of the alcohol problems continuum in college students: the Brief Young Adult Alcohol Consequences Questionnaire. Alcohol Clin Exp Res 29:1180–1189.

Table F-7. Brief interventions, substance use problem scale outcomes and effects

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	SMD (95% CI)	SNMD (95% CI)
27801991	Arnaud, 2017	MI	141 (3 mo)	Yes	11.26 (7.39)	4.45 (4.85)	-0.9 (-1.1 ,-0.7)	-0.15 (-0.4 ,0.1)
27801991	Arnaud, 2017	TAU	175 (3 mo)	Yes	9.72 (7.02)	4.05 (4.66)	-0.75 (-0.9 ,-0.6)	
29750362	Colby, 2018	MI	83 (3 mo)	Yes	8.46 (4.35)	4.76 (4.5)	-0.7 (-0.9 ,-0.5)	-0.5 (-0.8 ,-0.2)
29750362	Colby, 2018	TAU	84 (3 mo)	Yes	6.99 (4.48)	5.97 (4.09)	-0.19 (-0.4 ,0)	
30138016	D'Amico, 2018	MI	153 (3 mo)	Yes	6.59 (14.17)	2.17 (5.05)	-0.29 (-0.4 ,-0.1)	0 (-0.2 ,0.2)
30138016	D'Amico, 2018	TAU	141 (3 mo)	Yes	7.86 (16.57)	3.39 (9.03)	-0.29 (-0.5 ,-0.1)	
24969735	de Gee, 2014	MI	58 (3 mo)	Yes	6.2 (4.3)	6.2 (3.8)	0 (-0.3 ,0.3)	0 (-0.36 ,0.36)
24969735	de Gee, 2014	Educ	61 (3 mo)	Yes	5.7 (3.7)	5.7 (3.7)	0 (-0.2 ,0.2)	
17869051	Martin, 2008	MI	20 (3 mo)	Yes	5.8 (1.2)	3.8 (2.8)	-0.78 (-1.2 ,-0.3)	-0.54 (-1.2 ,0.1)
CN-01953820 (cochrane)	Giles, 2019	MI	181 (12 mo)	Yes	8.1 (9.9)	4.5 (5.3)	-0.17 (-0.15,- 0.19)	-0.07 (-0.11, -0.03)

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	SMD (95% CI)	SNMD (95% CI)
CN-01953820 (cochrane)	Giles, 2019	TAU	197 (12 mo)	Yes	6.5 (8.7)	4.0 (4.8)	-0.10 (-0.08, -0.12)	
17869051	Martin, 2008	TAU	20 (3 mo)	Yes	4.8 (2.1)	4.2 (2)	-0.23 (-0.7 ,0.2)	
18778385	McCambridge, 2008	MI	164 (3 mo)	Yes	6.5 (4.3)	5 (4.1)	-0.29 (-0.4 ,-0.1)	0.04 (-0.18 ,0.26)
18778385	McCambridge, 2008	Educ	162 (3 mo)	Yes	7 (4)	5.3 (4.3)	-0.33 (-0.5 ,-0.2)	
21688877	Walker, 2011	MI	101 (3 mo)	Yes	18.47 (13.47)	14.68 (10.39)	-0.27 (-0.5 ,-0.1)	-0.08 (-0.2 ,0.36)
21688877	Walker, 2011	Educ	100 (3 mo)	Yes	19.13 (12.31)	14.24 (10.18)	-0.34 (-0.5 ,-0.2)	
22000326	Winters, 2012	MI	257 (6 mo)	Yes	15.42 (4.37)	12.46 (2.82)	-0.64 (-0.8 ,-0.5)	-0.21 (-0.5 ,0.1)
22000326	Winters, 2012	TAU	56 (6 mo)	Yes	15.5 (4.8)	13.5 (3.1)	-0.43 (-0.7 ,-0.1)	
17563146	Winters, 2007	MI	52 (6 mo)	Yes	15.25 (1.5)	11.5 (1.41)	-1.85 (-2.1 ,-1.6)	-1.65 (-2.2 ,-1.1)
17563146	Winters, 2007	TAU	26 (6 mo)	Yes	14.3 (2)	13.9 (2.1)	-0.2 (-0.7 ,0.3)	

Abbreviations: PMID = PubMed ID (or other ID); N=number randomized;SD = standard deviation; End mean = mean at End; SMD = standardized mean difference; SNMD = standardized net mean difference (MI versus TAU or Educ); MI = motivational interviewing; Educ = psychoeducation; TAU = treatment as usual

Appendix G. Nonbrief Interventions: Detailed Results

Table G-1. Nonbrief interventions, alcohol use days

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	SMD (95% CI)
18072842	Baer, 2007	MI	75 (3 mo)	No	5.8 (6.8)	4.5 (7.1)	-1.3 (-3.2 ,0.6)	-0.17 (-0.4 ,0.1)
18072842	Baer, 2007	TAU	52 (3 mo)	No	4.8 (4.8)	2.9 (6.2)	-1.9 (-3.8 ,0)	-0.24 (-0.5 ,0)
CN-00917707 (Cochrane)	D'Amico, 2013	MI	109 (3 mo)	No	2.65 (1.72)	2.8 (1.6)	0.15 (-0.2 ,0.5)	0.08 (-0.1 ,0.3)
CN-00917707 (Cochrane)	D'Amico, 2013	PeerGroup	78 (3 mo)	No	2.31 (1.45)	2.24 (1.4)	-0.07 (-0.5 ,0.3)	-0.04 (-0.2 ,0.2)
12127465	Godley, 2002	TAU	51 (3 mo)	No	3.3 (6.07)	2.7 (6.07)	-0.6 (-2.6 ,1.4)	-0.08 (-0.4 ,0.2)
12127465	Godley, 2002	CBT+ICM	63 (3 mo)	No	4.2 (7.42)	1.5 (3.37)	-2.7 (-4.5 ,-0.9)	-0.37 (-0.6 ,-0.1)
20219293	Godley, 2010	TAU	80 (3 mo)	No	2.01 (2.84)	1.38 (2.08)	-0.63 (-1.3 ,0)	-0.25 (-0.5 ,0)
20219293	Godley, 2010	CBT+ICM	80 (3 mo)	No	1.14 (1.77)	1.11 (1.74)	-0.03 (-0.5 ,0.4)	-0.01 (-0.2 ,0.2)
20219293	Godley, 2010	CBT+MI	79 (3 mo)	No	1.2 (1.85)	1.29 (1.96)	0.09 (-0.4 ,0.6)	0.04 (-0.2 ,0.2)
20219293	Godley, 2010	CBT+MI+ICM	81 (3 mo)	No	1.35 (2.04)	1.2 (1.85)	-0.15 (-0.7 ,0.4)	-0.06 (-0.3 ,0.1)
16551142	Henggeler, 2006	Fam+CM+PeerGroup	37 (4 mo)	No	2.62 (5.43)	0.14 (0.33)	-2.48 (-4.2 ,-0.8)	-0.78 (-1.3 ,-0.2)
16551142	Henggeler, 2006	Fam+PeerGroup	29 (4 mo)	No	0.43 (1.11)	0.13 (0.3)	-0.3 (-0.7 ,0.1)	-0.09 (-0.2 ,0)
16551142	Henggeler, 2006	PeerGroup	64 (4 mo)	No	0.52 (0.87)	0.64 (1.98)	0.13 (-0.4 ,0.6)	0.04 (-0.1 ,0.2)
18705691	Liddle, 2008	CBT	112 (5 mo)	No	27.41 (15.65)	27.39 (19.71)	-0.02 (-4.1 ,4)	0 (-0.2 ,0.2)
18705691	Liddle, 2008	Fam	112 (5 mo)	No	28.47 (17.36)	19.75 (18.18)	-8.72 (-12.8 ,-4.7)	-0.4 (-0.6 ,-0.2)

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	SMD (95% CI)
19522781	Slesnick, 2009	TAU	42 (3 mo)	No	5.1 (3)	2.7 (3)	-2.4 (-3.5 ,-1.3)	-0.36 (-0.5 ,-0.2)
19522781	Slesnick, 2009	Fam	77 (3 mo)	No	7.63 (7.65)	2.23 (4.61)	-5.4 (-7.2 ,-3.6)	-0.81 (-1.1 ,-0.5)
25736623	Slesnick, 2015	MI	86 (3 mo)	No	5.01 (7.18)	2.55 (4.22)	-2.46 (-4 ,-0.9)	-0.34 (-0.6 ,-0.1)
25736623	Slesnick, 2015	CBT	93 (3 mo)	No	4.53 (7.03)	3.11 (4.7)	-1.42 (-2.9 ,0.1)	-0.2 (-0.4 ,0)
25736623	Slesnick, 2015	ICM	91 (3 mo)	No	3.73 (5.51)	3.04 (5.51)	-0.69 (-2.1 ,0.7)	-0.1 (-0.3 ,0.1)
24841864	Wagner, 2014	TAU	235 (4 mo)	No	2.28 (2.56)	1.61 (1.89)	-0.67 (-1 ,-0.3)	-0.24 (-0.4 ,-0.1)
24841864	Wagner, 2014	CBT+MI	279 (4 mo)	No	2.42 (2.77)	1.01 (1.62)	-1.41 (-1.7 ,-1.1)	-0.5 (-0.6 ,-0.4)
26992083	Henderson, 2016	TAU	63 (3 mo)	Yes	0.18 (0.16)	0.04 (0.09)		-0.82 (-1.1 ,-0.6)
26992083	Henderson, 2016	CBT+ICM	63 (3 mo)	Yes	0.23 (0.18)	0.04 (0.09)		-1.12 (-1.4 ,-0.9)
2017-00657-001 (psycINFO)	Trudeau, 2017	TAU	69 (3 mo)	Yes	85.18 (43.08)	82 (31.47)		-0.07 (-0.3 ,0.2)
2017-00657-001 (psycINFO)	Trudeau, 2017	CBT	48 (3 mo)	Yes	103.58 (43.19)	81.59 (31.65)		-0.49 (-0.8 ,-0.2)

Abbreviations: PMID = PubMed ID (or other ID), N=number randomized;SD = standard deviation;End mean = mean at End;MD = mean difference; SMD = standardized mean difference; MI = motivational interviewing; Fam = family therapy; CBT = cognitive behavioral therapy; PeerGroup = peer group therapy; Educ = psychoeducation; CM = contingency management; ICM = intensive case management; TAU = treatment as usual

Table G-2. Nonbrief interventions, cannabis use days

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	SMD (95% CI)
18072842	Baer, 2007	MI	75 (3 mo)	No	17.4 (11.5)	14.8 (12.2)	-2.6 (-5.9 ,0.7)	-0.18 (-0.4 ,0)
18072842	Baer, 2007	TAU	52 (3 mo)	No	19.1 (11.1)	13.2 (12.4)	-5.9 (-9.8 ,-2)	-0.41 (-0.7 ,-0.1)
CN-00917707 (Cochrane)	D'Amico, 2013	MI	109 (3 mo)	No	3.15 (2.36)	2.75 (1.23)	-0.4 (-0.8 ,0)	-0.16 (-0.3 ,0)
CN-00917707 (Cochrane)	D'Amico, 2013	PeerGroup	78 (3 mo)	No	2.96 (2.22)	2.38 (2.03)	-0.58 (-1.2 ,0)	-0.24 (-0.5 ,0)
12127465	Godley, 2002	TAU	51 (3 mo)	No	10.8 (10.93)	5.7 (9.11)	-5.1 (-8.5 ,-1.7)	-0.41 (-0.7 ,-0.1)
12127465	Godley, 2002	CBT+ICM	63 (3 mo)	No	12 (12.15)	4.2 (8.1)	-7.8 (-11 ,-4.6)	-0.62 (-0.9 ,-0.4)
16551142	Henggeler, 2006	Fam+CM+PeerGroup	37 (4 mo)	No	11.57 (9.99)	2.32 (6.6)	-9.24 (-12.6 ,-5.9)	-0.98 (-1.3 ,-0.6)
16551142	Henggeler, 2006	Fam+PeerGroup	29 (4 mo)	No	11.29 (9.25)	1.21 (2.99)	-10.08 (-13.4 ,-6.8)	-1.07 (-1.4 ,-0.7)
16551142	Henggeler, 2006	PeerGroup	64 (4 mo)	No	8.88 (8.31)	2.75 (6.65)	-6.13 (-8.4 ,-3.9)	-0.65 (-0.9 ,-0.4)
12957348	Latimer, 2003	Educ	22 (5 mo)	No	16.55 (11.48)	14.1 (11.49)	-2.45 (-8.3 ,3.4)	-0.19 (-0.7 ,0.3)
12957348	Latimer, 2003	CBT+Fam	21 (5 mo)	No	15.86 (10.38)	6.19 (8.66)	-9.67 (-14.7 ,-4.6)	-0.76 (-1.2 ,-0.4)
18705691	Liddle, 2008	CBT	112 (5 mo)	No	11.89 (12.71)	9.83 (15.56)	-2.06 (-5.3 ,1.2)	-0.14 (-0.4 ,0.1)
18705691	Liddle, 2008	Fam	112 (5 mo)	No	10.41 (11.38)	5.12 (8.3)	-5.29 (-7.6 ,-3)	-0.35 (-0.5 ,-0.2)
15152709	Liddle, 2004	CBT	43 (3.5 mo)	No	4.21 (4.84)	4.31 (7.11)	0.1 (-2.2 ,2.4)	0.01 (-0.3 ,0.4)
15152709	Liddle, 2004	Fam	40 (3.5 mo)	No	3.05 (5.65)	0.68 (3.64)	-2.37 (-4.2 ,-0.5)	-0.35 (-0.6 ,-0.1)
23140805	Rigter, 2013	TAU	238 (3 mo)	No	19.93 (8.43)	13.13 (10.83)	-6.8 (-8.3 ,-5.3)	-0.58 (-0.7 ,-0.5)

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	SMD (95% CI)
23140805	Rigter, 2013	Fam	212 (3 mo)	No	20.5 (8.47)	15.07 (10.07)	-5.43 (-7 ,-3.9)	-0.47 (-0.6 ,-0.3)
26004659	Stanger, 2015	CBT+MI	38 (3 mo)	No	1.3 (1)	1.2 (0.9)	-0.1 (-0.5 ,0.3)	-0.08 (-0.4 ,0.2)
26004659	Stanger, 2015	CBT+MI+CM	80 (3 mo)	No	1.15 (1.05)	1.35 (1.11)	0.2 (-0.1 ,0.5)	0.16 (-0.1 ,0.4)
CN-01365355 (Cochrane)	Tolou-Shams, 2017	Educ	22 (3 mo)	No	5.12 (8.26)	6.48 (10.63)	1.36 (-3.5 ,6.3)	0.1 (-0.3 ,0.5)
CN-01365355 (Cochrane)	Tolou-Shams, 2017	CBT+Fam	25 (3 mo)	No	12.21 (13.38)	8.75 (12.38)	-3.47 (-9.7 ,2.7)	-0.25 (-0.7 ,0.2)
11680557	Waldron, 2001	Educ	30 (4 mo)	No	19.86 (8.11)	16.72 (10.46)	-3.14 (-7.3 ,1)	-0.26 (-0.6 ,0.1)
11680557	Waldron, 2001	CBT+MI	31 (4 mo)	No	15.66 (9.71)	15.63 (12.03)	-0.03 (-4.8 ,4.7)	0 (-0.4 ,0.4)
11680557	Waldron, 2001	CBT+MI+Fam	29 (4 mo)	No	17.02 (10.49)	11.42 (10.95)	-5.59 (-10.4 ,-0.8)	-0.46 (-0.9 ,-0.1)
11680557	Waldron, 2001	Fam	30 (4 mo)	No	16.46 (9.81)	7.49 (8.09)	-8.98 (-12.9 ,-5)	-0.74 (-1.1 ,-0.4)

Abbreviations: PMID = PubMed ID (or other ID), N=number randomized;SD = standard deviation;End mean = mean at End;MD = mean difference; SMD = standardized mean difference; MI = motivational interviewing; Fam = family therapy; CBT = cognitive behavioral therapy; PeerGroup = peer group therapy; Educ = psychoeducation; CM = contingency management; ICM = intensive case management; TAU = treatment as usual

Table G-3. Nonbrief interventions, alcohol and other drug use days

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	SMD (95% CI)
CN-00241903 (Cochrane)	Azrin, 1994	CBT	15 (6 mo)	No	6.6 (7.4)	2.3 (2.9)	-4.3 (-8 ,-0.6)	-0.58 (-1.1 ,-0.1)
CN-00241903 (Cochrane)	Azrin, 1994	PeerGroup	11 (6 mo)	No	6.8 (5.3)	8.5 (8.1)	1.7 (-3.3 ,6.7)	0.23 (-0.4 ,0.9)
25621927	Dakof, 2015	CBT+MI	57 (6 mo)	No	22.27 (13.94)	7.72 (13.96)	-14.55 (-19 ,-10.1)	-0.9 (-1.2 ,-0.6)
25621927	Dakof, 2015	Fam	55 (6 mo)	No	20.62 (14.42)	4.96 (10.54)	-15.66 (-19.8 ,-11.5)	-0.97 (-1.2 ,-0.7)
20219293	Godley, 2010	TAU	80 (3 mo)	No	9.12 (8.99)	7.08 (7.56)	-2.04 (-4.3 ,0.2)	-0.24 (-0.5 ,0)
20219293	Godley, 2010	CBT+ICM	80 (3 mo)	No	7.68 (7.98)	4.11 (5.09)	-3.57 (-5.4 ,-1.7)	-0.42 (-0.6 ,-0.2)
20219293	Godley, 2010	CBT+MI	79 (3 mo)	No	6.57 (7.19)	4.38 (5.35)	-2.19 (-3.9 ,-0.5)	-0.26 (-0.5 ,-0.1)
20219293	Godley, 2010	CBT+MI+ICM	81 (3 mo)	No	7.32 (7.73)	3.63 (4.62)	-3.69 (-5.4 ,-2)	-0.43 (-0.6 ,-0.2)
25496283	Hogue, 2015	TAU	79 (3 mo)	No	6.2 (9.2)	6.8 (8.7)	0.6 (-1.7 ,2.9)	0.06 (-0.2 ,0.3)
25496283	Hogue, 2015	Fam	75 (3 mo)	No	6.6 (8.5)	8.9 (9.9)	2.3 (-0.1 ,4.7)	0.22 (0 ,0.5)
29866383	Liddle, 2018	TAU	53 (4 mo)	No	27.57 (18.01)	5.07 (10.7)	-22.5 (-27.4 ,-17.6)	-1.24 (-1.5 ,-1)
29866383	Liddle, 2018	Fam	55 (4 mo)	No	33.4 (19.05)	5.31 (7.74)	-28.09 (-32.9 ,-23.2)	-1.55 (-1.8 ,-1.3)
16989957	Slesnick, 2007	TAU	84 (6 mo)	No	18 (10.2)	15 (10.8)	-3 (-5.8 ,-0.2)	-0.23 (-0.4 ,0)
16989957	Slesnick, 2007	CBT	96 (6 mo)	No	20.1 (9.9)	12.9 (11.1)	-7.2 (-9.8 ,-4.6)	-0.56 (-0.8 ,-0.4)
25736623	Slesnick, 2015	MI	86 (3 mo)	No	20.51 (10.86)	13.7 (13.03)	-6.81 (-9.9 ,-3.7)	-0.47 (-0.7 ,-0.3)
25736623	Slesnick, 2015	CBT	93 (3 mo)	No	17.63 (11.8)	16.08 (12.23)	-1.55 (-4.5 ,1.4)	-0.11 (-0.3 ,0.1)

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	SMD (95% CI)
25736623	Slesnick, 2015	ICM	91 (3 mo)	No	16.64 (10.4)	14.81 (12.2)	-1.83 (-4.7 ,1)	-0.13 (-0.3 ,0.1)
9824170	Kaminer, 1998	CBT	16 (3 mo)	Yes	3.5 (1.83)	1.5 (1.08)		-0.88 (-1.3 ,-0.5)
9824170	Kaminer, 1998	PeerGroup	16 (3 mo)	Yes	4.33 (1.67)	3.13 (2.64)		-0.53 (-1.1 ,0.1)

Abbreviations: PMID = PubMed ID (or other ID); N=number randomized ;SD = standard deviation; End mean = mean at End; MD = mean difference; SMD = standardized mean difference; MI = motivational interviewing; Fam = family therapy; CBT = cognitive behavioral therapy; PeerGroup = peer group therapy; Educ = psychoeducation; CM = contingency management; ICM = intensive case management; TAU = treatment as usual

Table G-4. Nonbrief interventions, illicit drug use days

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	SMD (95% CI)
2002-13926-001 (psycINFO)	Azrin, 2001	CBT	27 (6 mo)	No	14.14 (10.58)	9.28 (10.23)	-4.86 (-9.7 ,-0.1)	-0.41 (-0.8 ,0)
2002-13926-001 (psycINFO)	Azrin, 2001	Fam	29 (6 mo)	No	13.62 (10.3)	9 (8.33)	-4.62 (-8.8 ,-0.4)	-0.39 (-0.7 ,0)
21967492	Robbins, 2011	TAU	179 (4 mo)	No	3.21 (1.61)	2.14 (1.25)	-1.07 (-1.3 ,-0.8)	-0.63 (-0.8 ,-0.5)
21967492	Robbins, 2011	Fam	194 (4 mo)	No	3.21 (1.79)	1.07 (1.25)	-2.14 (-2.4 ,-1.9)	-1.26 (-1.4 ,-1.1)
19522781	Slesnick, 2009	TAU	34 (3 mo)	No	11.4 (7.5)	7.5 (8.4)	-3.9 (-7 ,-0.8)	-0.39 (-0.7 ,-0.1)
19522781	Slesnick, 2009	Fam	63 (3 mo)	No	12.9 (9.29)	7.24 (8.39)	-5.66 (-8.2 ,-3.1)	-0.57 (-0.8 ,-0.3)
24841864	Wagner, 2014	TAU	235 (4 mo)	No	4.49 (7.46)	3.72 (8.08)	-0.77 (-2 ,0.4)	-0.09 (-0.2 ,0)
24841864	Wagner, 2014	CBT+MI	279 (4 mo)	No	5.87 (8.43)	2.06 (5.01)	-3.81 (-4.8 ,-2.8)	-0.42 (-0.5 ,-0.3)
30556713	Zhang, 2018	MI	86 (3 mo)	No	20.45 (10.86)	13.7 (12.97)	-6.75 (-9.9 ,-3.6)	-0.47 (-0.7 ,-0.3)

PMID	Citation	Intervention	N (endtime)	Scale	Baseline Mean (SD)	End Mean (SD)	MD (95% CI)	SMD (95% CI)
30556713	Zhang, 2018	CBT	93 (3 mo)	No	17.97 (11.67)	16.08 (12.23)	-1.89 (-4.9 ,1.1)	-0.13 (-0.3 ,0.1)
30556713	Zhang, 2018	ICM	91 (3 mo)	No	17.04 (10.46)	14.81 (12.2)	-2.23 (-5.1 ,0.6)	-0.16 (-0.4 ,0)
11727882	Liddle, 2001	Fam	100 (5.5 mo)	Yes	9.96 (3.61)	6.1 (4.28)		-0.86 (-1.1 ,-0.6)
11727882	Liddle, 2001	PeerGroup	52 (5.5 mo)	Yes	8.83 (2.76)	7.33 (3.41)		-0.33 (-0.6 ,-0.1)
2017-00657-001 (psyclNFO)	Trudeau, 2017	TAU	80 (3 mo)	Yes	56.77 (14.75)	59.08 (12.01)		0.14 (-0.1 ,0.4)
2017-00657-001 (psyclNFO)	Trudeau, 2017	CBT	49 (3 mo)	Yes	57.78 (15.96)	57.13 (11.38)		-0.04 (-0.3 ,0.2)

Abbreviations: PMID = PubMed ID (or other ID); N=number randomized ;SD = standard deviation; End mean = mean at End; MD = mean difference; SMD = standardized mean difference; MI = motivational interviewing; Fam = family therapy; CBT = cognitive behavioral therapy; PeerGroup = peer group therapy; Educ = psychoeducation; CM = contingency management; ICM = intensive case management; TAU = treatment as usual

Table G-5. School performance, and educational attainment outcomes with nonbrief behavioral interventions

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI
Kaminer 1998 [139, 140]	CBT (delivery group)	Peer Group (delivery group)	School Problems	T-ASI	0	16	1.27 (1.10)	16	1.75 (1.36)	-
			School Problems	T-ASI	3	16	1.22 (0.97)	16	1.71 (1.6)	Net Diff -0.01 (-0.9, 0.88)
Kaminer 2002 [141-143]	Educational (delivery group)	CBT (delivery group)	School Problems	T-ASI	0	37	1.6 (1.2)	51	1.6 (1.4)	-
			School Problems	T-ASI	3	37	1.6 (1.5)	51	1.3 (1.4)	Net Diff 0.3 (-0.57, 1.17)
			School Problems	T-ASI	9	37	0.8 (1.1)	51	0.9 (1.0)	Net Diff -0.1 (-0.76, 0.56)

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI
Liddle 2004 [152-154]	CBT + Peer Group (delivery group)	Family Therapy (ecological)	School problems - Academic	Adolescent interview	0	39	5.38 (1.19)	41	5.71 (1.31)	-
			School problems - Academic	Adolescent interview	1.5	39	5.33 (1.25)	41	5.18 (1.13)	Net Diff 0.48 (-0.06, 1.02)
			School problems - Academic	Adolescent interview	3-4	39	4.78 (1.07)	41	4.86 (1.03)	Net Diff 0.25 (-0.26, 0.76)
			School problems - Discipline	Adolescent interview	0	39	8.18 (1.87)	41	8.37 (1.81)	-
			School problems - Discipline	Adolescent interview	1.5	39	7.53 (1.37)	41	7.33 (1.53)	Net Diff 0.39 (-0.35, 1.13)
			School problems - Discipline	Adolescent interview	3-4	39	7.58 (1.55)	41	7.09 (1.29)	Net Diff 0.68 (-0.05, 1.41)
Azrin 2001 2002-[112]	CBT (integrated intervention)	Family Therapy (behavioral; integrated intervention)	School performance	PHYS	0	27	23.70 (31.88)	29	20.06 (25.50)	-
			School performance	PHYS	6	27	57.52 (32.78)	29	67.93 (23.51)	Net Diff -14.05 (-29.17, 1.07)
			School performance	PHYS	12	27	60.61 (27.25)	29	65.74 (26.90	Net Diff -8.77 (-23.53, 5.99)
			School performance	YHPS	0	27	33.78 (7.80)	29	32.32 (8.01)	-
			School performance	YHPS	6	27	37.89 (11.30)	29	38.05 (11.02)	Net Diff -1.62 (-6.83, 3.59)
			School performance	YHPS	12	27	36.85 (9.15)	29	40.00 (10.63)	Net Diff -4.61 (-9.36, 0.14)
			School performance	LSS-A	0	27	65.35 (31.89)	29	63.60 (30.61)	-

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI
			School performance	LSS-A	6	27	87.41 (17.45)	29	78.28 (23.77)	Net Diff 7.38 (-7.16, 21.92)
			School performance	LSS-A	12	27	83.81 (23.90)	29	79.24 (25.01)	Net Diff 2.82 (-12.12, 17.76)
Schaeffer 2013 [185]	NOS + Apprentice training	TAU	Educational attainment	Enrollment in a GED program	0	-	-	-	-	-
			Educational attainment	Enrollment in a GED program	30	50	50.0%	47	26.1%	**OR* 2.85 (95% CI, 1.20 to 6.75)**
			Educational attainment	Graduation from high school	0	-	-	-	-	-
			Educational attainment	Graduation from high school	30	50	14.0%	47	23.4%	OR 0.53 (95% CI, 0.19, 1.52)

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; Diff = difference; GED = General Equivalency Diploma; LSS-A = Life Satisfaction Scale for Adolescents; N = number randomized; Net Diff = difference between in Intervention and Control groups in the mean change from baseline (time 0); NOS = not otherwise specified; OR = odds ratio; PHYS = Parent Happiness with Youth Scale; PMID = Pubmed ID; T-ASI = Teen Addiction Severity Index; TAU = treatment as usual; YHPS = Youth Happiness with Parent Scale.
Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences.

Table G-6. Family-related outcomes with nonbrief behavioral interventions

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI
Kaminer 1998 [139, 140]	CBT (delivery group)	Peer Group (delivery group)	Family Problems	T-ASI	0	16	1.77 (0.93)	16	1.83 (1.03)	-
			Family Problems	T-ASI	3	16	0.90 (0.74)	16	1.63 (0.74)	**Net Diff -0.67 (-1.28, -0.06)**
Kaminer 2002 [141-143]	Educational (delivery group)	CBT (delivery group)	Family Problems	T-ASI	0	37	1.4 (1.1)	51	1.5 (0.9)	-
			Family Problems	T-ASI	3	37	1.0 (1.0)	51	0.8 (0.9)	Net Diff 0.3 (-0.12, 0.72)
			Family Problems	T-ASI	9	37	0.7 (1.1)	51	0.5 (0.7)	Net Diff 0.3 (-0.12, 0.72)
Liddle 2004 [152-154]	CBT + Peer Group (delivery group)	Family Therapy (ecological)	Family Problems – Family Cohesion	FES	0	39	11.24 (1.67)	41	11.89 (2.39)	-
			Family Problems – Family Cohesion	FES	1.5	39	11.17 (2.02)	41	11.02 (2.11)	Net Diff 0.8 (-0.11, 1.71)
			Family Problems – Family Cohesion	FES	3-4	39	11.54 (2.15)	41	10.94 (1.91)	**Net Diff 1.25 (0.34, 2.16)**
			Family Problems – Family Conflict	FES	0	39	11.24 (1.67)	41	14.53 (2.01)	-
			Family Problems – Family Conflict	FES	1.5	39	11.17 (2.02)	41	15.26 (2.05)	Net Diff -0.8 (-1.65, 0.05)

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI
			Family Problems – Family Conflict	FES	3-4	39	11.54 (2.15)	41	15.20 (2.24)	Net Diff -0.37 (-1.27, 0.53)
			Positive Family Interactions	ADI	0	43	13.75 (2.23)	40	13.83 (2.07)	-
			Positive Family Interactions	ADI	1.5	43	15.03 (2.04)	40	14.36 (2.34)	Net Diff 0.75 (-0.19, 1.69)
			Positive Family Interactions	ADI	3-4	43	15.17 (2.02)	40	14.26 (2.18)	**Net Diff 0.99 (0.07, 1.91)**
			Positive Family Interactions	ADI	6	43	15.07 (2.28)	40	14.85 (2.36)	Net Diff 0.3 (-0.67, 1.27)
			Positive Family Interactions	ADI	12	43	14.88 (2.31)	40	15.16 (2.01)	Net Diff -0.2 (-1.13, 0.73)
			Negative Family Interactions	ADI	0	43	7.15 (0.90)	40	7.33 (1.15)	-
			Negative Family Interactions	ADI	1.5	43	7.30 (0.88)	40	7.46 (0.75)	Net Diff 0.02 (-0.39, 0.43)
			Negative Family Interactions	ADI	3-4	43	7.60 (0.65)	40	7.38 (0.74)	**Net Diff 0.4 (0.01, 0.79)**
			Negative Family Interactions	ADI	6	43	7.61 (0.60)	40	7.43 (0.78)	Net Diff 0.36 (-0.03, 0.75)
			Negative Family Interactions	ADI	12	43	7.69 (0.52)	40	7.53 (0.72)	Net Diff 0.34 (-0.05, 0.73)
Santisteban 2011 [183]	MI + Educ + Fam (culturally tailored)	Fam (structural)	Family problems – Parent-reported composite	PPQ	0	12	7.70 (0.90)	13	7.64 (1.28)	-

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI
			Family problems – Parent-reported composite	PPQ	8	12	8.00 (1.10)	13	7.49 (1.14)	Net Diff 0.45 (-0.43, 1.33)
			Family problems – Parent-reported composite	PPQ	0	12	6.08 (2.09)	13	6.26 (1.52)	-
			Family problems – Parent-reported composite	PPQ	8	12	7.45 (1.54)	13	5.89 (1.89)	**Net Diff 1.74 (0.32, 3.16)**
Robbins 2011 172-179	Fam (structural)	TAU	Family Functioning	Composite of PPQ and FES	0	245	-0.03 (1.01)	235	0.04 (0.99)	-
			Family Functioning	Composite of PPQ and FES	4	194	0.15 (1.02)	188	0.21 (0.94)	Net Diff 0.01 (-0.18, 0.2)
			Family Functioning	Composite of PPQ and FES	8	169	0.31 (0.96)	164	0.25 (0.97)	Net Diff 0.13 (-0.06, 0.32)
			Family Functioning	Composite of PPQ and FES	12	169	0.35 (0.96)	158	0.14 (0.99)	**Net Diff 0.28 (0.08, 0.48)**

Abbreviations: ADI = Adolescent Diagnostic Interview; CBT = cognitive behavioral therapy; CI = confidence interval; FES = Family Environment Scale; MI = motivational interviewing; Net Diff = difference between in Intervention and Control groups in the mean change from baseline (time 0); N = number randomized; NOS = not otherwise specified; PMID = Pubmed ID; PPQ = Parenting Practices Questionnaire; OR = odds ratio; T-ASI = Teen Addiction Severity Index; TAU = treatment as usual.
Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences

Table G-7. Peer-related outcomes with nonbrief behavioral interventions

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome	Calculated Effect (95% CI
Kaminer 1998 [139, 140]	CBT (delivery group)	Peer Group (delivery group)	Peer Problems	T-ASI	0	16	1.08 (1.31)	16	1.58 (0.79)	-
			Peer Problems	T-ASI	3	16	1.30 (1.25)	16	1.38 (0.92)	Net Diff 0.42 (-0.34, 1.18)
Kaminer 2002 [141-143]	Educational (delivery group)	CBT (delivery group)	Peer Problems	T-ASI	0	37	0.5 (0.8)	51	0.6 (0.7)	-
			Peer Problems	T-ASI	3	37	0.6 (0.6)	51	0.5 (0.6)	Net Diff 0.2 (-0.09, 0.49)
			Peer Problems	T-ASI	9	37	0.5 (0.5)	51	0.5 (0.8)	Net Diff 0.1 (-0.19, 0.39)
Liddle 2004 [152-154]	CBT + Peer Group (delivery group)	Family Therapy (ecological)	Peer problems	Affiliation with delinquent peers	0	43	100.26 (15.45)	40	99.07 (15.90)	-
			Peer problems	Affiliation with delinquent peers	1.5	43	114.67 (14.11)	40	112.28 (12.38)	Net Diff 1.2 (-5.1, 7.5)
			Peer problems	Affiliation with delinquent peers	3-4	43	105.23 (14.52)	40	113.11 (4.80)	**Net Diff -9.07 (-15.34, -2.8)**
			Peer problems	Affiliation with delinquent peers	6	43	109.52 (9.57)	40	113.50 (3.47)	Net Diff -5.17 (-11.21, 0.87)
			Peer problems	Affiliation with delinquent peers	12	43	106.27 (20.14)	40	112.56 (8.13)	**Net Diff -7.48 (-14.41, -0.55)**

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; Diff = difference; N = number randomized; Net Diff = difference between in Intervention and Control groups in the mean change from baseline (time 0); NOS = not otherwise specified; OR = odds ratio; PMID = Pubmed ID; T-ASI = Teen Addiction Severity Index; TAU = treatment as usual. Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences

Table G-8. Mental health outcomes with nonbrief behavioral interventions

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome
Kaminer 2008 [144-146]	CBT + in-person MI	CBT + brief telephone MI	Suicidal ideation	0	38	12.2 (9.0)	43	8.8 (6.9)	-
			Suicidal ideation	3	38	13.1 (15.3)	43	7.4 (7.2)	Net Diff 2.3 (-2.4, 7.0)
			Suicidal ideation	7	38	8.8 (6.5)	43	6.1 (5.9)	Net Diff -0.7 (-3.8, 2.4)
	CBT + in-person MI	TAU	Suicidal ideation	0	38	12.2 (9.0)	41	8.6 (6.4)	-
			Suicidal ideation	3	38	13.1 (15.3)	41	10.6 (7.0)	Net Diff -1.1 (-5.8, 3.6)
			Suicidal ideation	7	38	8.8 (6.5)	41	7.0 (7.7)	Net Diff -1.8 (-5.2, 1.6)
	CBT + brief telephone MI	TAU	Suicidal ideation	0	43	8.8 (6.9)	41	8.6 (6.4)	-
			Suicidal ideation	3	43	7.4 (7.2)	41	10.6 (7.0)	Net Diff -3.4 (-6.3, -0.5)
			Suicidal ideation	7	43	6.1 (5.9)	41	7.0 (7.7)	Net Diff -1.1 (-4.0, 1.8)
Esposito-Smythers 2011 [120]	Family (integrated intervention)	TAU (delivery group, integrated intervention)	Suicide attempt	18	19	5%	17	35%	**OR 0.10 (0.01, 0.96)**
			Residential placement	18	19	3%	17	21%	OR 0.10 (0.01, 2.19)
			Hospitalization	18	19	16%	17	53%	
			Partial hospitalization	18	19	5%	17	24%	OR 0.18 (0.02, 1.81)

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; MI = motivational interviewing; N = number; Net Diff = difference between in Intervention and Control groups in the mean change from baseline (time 0); OR = odds ratio; PMID = Pubmed ID; TAU = treatment as usual. **Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences.**

Table G-9. Physical health outcomes with nonbrief behavioral interventions

Author (Year) PMID	Arm 1	Arm 2	Outcome	Measurement	Timepoint (Months)	Arm 1 N Analyzed	Arm 1 Outcome	Arm 2 N Analyzed	Arm 2 Outcome
Rowe 2016 [182]	CBT+MI (integrated intervention, parent)	TAU	Testing positive for STI	0	76	9%	78	12%	-
			Testing positive for STI	3	76	7%	78	8%	OR 0.85 (0.25, 2.89)
			Testing positive for STI	6	76	4%	78	6%	OR 0.60 (0.14, 2.60)
			Testing positive for STI	9	76	1%	78	5%	OR 0.25 (0.03, 2.26)
			Testing positive for STI	18	76	3%	78	5%	OR 0.50 (0.09, 2.81)
			Testing positive for STI	24	76	5%	78	5%	OR 1.03 (0.25, 4.27)
			Testing positive for STI	36	76	8%	78	5%	OR 1.59 (0.43, 5.86)
			Testing positive for STI	42	76	4%	78	6%	OR 0.60 (0.14, 2.60)
Esposito-Smythers 2011 [182]	Fam (integrated intervention)	TAU (delivery group, integrated intervention)	Emergency department visit	0	-	-	-	-	-
			Emergency department visit	18	19	16%	17	59%	**OR 0.13 (0.03, 0.63)**

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; MI = motivational interviewing; N = number; OR = odds ratio; PMID = Pubmed ID; STI = sexually transmitted infection; TAU = treatment as usual.

Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences.

Table G-10. Arrests and convictions (legal outcomes) with nonbrief behavioral interventions

Author (Year) PMID	Arm 1 (N)	Arm 2 (N)	Time (mo)	Arrests Int.	Arrests Cont.	Arrests Calc. Effect (95% CI)	Convictions for Person Crimes Int.	Convictions for Person Crimes Cont.	Convictions for Person Crimes Calc. Effect (95% CI)	Convictions for Property Crimes Int.	Convictions for Property Crimes Cont.	Convictions for Property Crimes Calc. Effect (95% CI)
Henggeler 2006 [134]	Fam (drug court + multisystemic therapy + contingency) (N=43)	Fam (drug court + multisystemic therapy) (N=38)	12	1.28 (1.44)	1.40 (1.52)	Mean Diff -0.12 (-0.78, 0.54)	-	-	-	-	-	-
	Fam (drug court + multisystemic therapy + contingency) (N=43)	TAU (family court + community services) (N=42)	12	1.28 (1.44)	1.00 (1.15)	Mean Diff 0.28 (-0.28, 0.84)	-	-	-	-	-	-
	Fam (drug court + multisystemic therapy + contingency) (N=43)	TAU (drug court + community services) (N=38)	12	1.28 (1.44)	1.45 (1.35)	Mean Diff -0.17 (-0.79, 0.45)	-	-	-	-	-	-
	Fam (drug court + multisystemic therapy) (N=38)	TAU (family court + community services) (N=42)	12	1.40 (1.52)	1.00 (1.15)	Mean Diff 0.40 (-0.20, 1.00)	-	-	-	-	-	-
	Fam (drug court + multisystemic therapy) (N=38)	TAU (drug court + community services) (N=38)	12	1.40 (1.52)	1.45 (1.35)	Mean Diff -0.05 (-0.71, 0.61)	-	-	-	-	-	-
	TAU (family court + community services) (N=42)	TAU (drug court + community services) (N=38)	12	1.00 (1.15)	1.45 (1.35)	Mean Diff -0.45 (-1.00, 0.11)	-	-	-	-	-	-
Dakof 2015 [118]	CBT+MI (delivery group) (N=57)	Fam (ecological) (N=55)	0	2.11 (1.18)	1.87 (0.94)	-	-	-	-	-	-	-
			6	0.32 (0.69)	0.47 (0.77)	Net Diff -0.39 (-0.74, -0.04)	-	-	-	-	-	-
			24	1.19 (1.54)	0.95 (1.24)	Net Diff 0.00 (-0.47, 0.47)	-	-	-	-	-	-
Azrin 2001 [112]	CBT (integrated intervention) (N=27)	Fam (behavioral; integrated intervention) (N=29)	0	0.84 (1.02)	0.93 (1.51)	-	-	-	-	-	-	-

Author (Year) PMID	Arm 1 (N)	Arm 2 (N)	Time (mo)	Arrests Int.	Arrests Cont.	Arrests Calc. Effect (95% CI)	Convictions for Person Crimes Int.	Convictions for Person Crimes Cont.	Convictions for Person Crimes Calc. Effect (95% CI)	Convictions for Property Crimes Int.	Convictions for Property Crimes Cont.	Convictions for Property Crimes Calc. Effect (95% CI)
			6	0.42 (0.82)	0.28 (0.48)	Net Diff 0.23 (-0.37, 0.83)	-	-	-	-	-	-
			12	0.24 (0.29)	0.51 (0.59)	Net Diff -0.18 (-0.77, 0.41)	-	-	-	-	-	-
Henggeler 2001 [129-133]	Fam (ecological) (N=58)	TAU (delivery group) (N=59)	11	40%	53%	OR 0.76 (0.51, 1.13)	-	-	-	-	-	-
			48	-	-	-	0.15 (0.43)	0.57 (1.80)	Mean Diff -0.42 (-0.90, 0.06)	0.19 (0.43)	0.20 (0.61)	Mean Diff -0.01 (-0.20, 0.18)
Esposito-Smythers 2011 [120]	Fam (structural) (N=19)	TAU (N=17)	18	5%	41%	OR 0.08 (0.01, 0.74)	-	-	-	-	-	-

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; MI = motivational interviewing; N = number; OR = odds ratio; PMID = Pubmed ID; STI = sexually transmitted infection; TAU = treatment as usual.

Bold font indicates that the 95% CI does not contain 1 for ORs or 0 for differences.

Table G-11. Self-reported legal outcomes with nonbrief behavioral interventions

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
Liddle 2004 [152-154]	CBT + Peer Group (delivery group) (N=43)	Family Therapy (ecological) (N=40)	0	51%	48%	-	-	-	-	-	-	-	-	-	-
			1.5	33%	10%	OR 4.4 (1.3, 14.6)	-	-	-	-	-	-	-	-	-
			3 to 4	33%	15%	OR 2.7 (0.9, 8.0)	-	-	-	-	-	-	-	-	-
			6	30%	28%	OR 1.1 (0.4. 3.0)	-	-	-	-	-	-	-	-	-
			12	33%	23%	OR 1.7 (0.6, 4.4)	-	-	-	-	-	-	-	-	-
Hogue 2015 [138]	Fam (structural) (N=104)	TAU (N=101)	0	3.6 (3.1)	3.9 (2.8)	-	-	-	-	-	-	-	-	-	-
			3	3.5 (2.5)	3.1 (2.6)	Net Diff 0.7 (-0.1, 1.5)	-	-	-	-	-	-	-	-	-
			6	2.3 (1.7)	3.0 (2.1)	Net Diff -0.4 (-1.1, 0.3)	-	-	-	-	-	-	-	-	-
			12	2.5 (2.5)	2.7 (2.6)	Net Diff -0.1 (-0.9, 0.7)	-	-	-	-	-	-	-	-	-
Kaminer 1998 [139, 140]	CBT (delivery group) (N=16)	Peer Group (delivery group) (N=16)	0	1.33 (1.15)	0.75 (1.22)	-	-	-	-	-	-	-	-	-	-
			3	0.90 (1.20)	1 (1.31)	Net Diff -0.7 (-1.5, 0.2)	-	-	-	-	-	-	-	-	-

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
Kaminer 2002 [141-143]	Educational (delivery group) (N=37)	CBT (delivery group) (N=51)	0	1.2 (1.1)	1.2 (1.1)	-	-	-	-	-	-	-	-	-	-
			3	0.6 (0.9)	0.7 (1.1)	Net Diff -0.1 (-0.5, 0.3)	-	-	-	-	-	-	-	-	-
			9	0.2 (0.4)	0.3 (0.7)	Net Diff -0.1 (-0.5, 0.3)	-	-	-	-	-	-	-	-	-
Azrin 2001 2002-[112]	CBT (integrated intervention) (N=27)	Family Therapy (behavioral; integrated intervention) (N=29)	0 (CBCL)	77.40 (8.45)	74.44 (6.70)	-									
			6 (CBCL)	66.67 (12.11)	63.55 (9.10)	Net Diff 0.2 (-4.9, 5.2)	-	-	-	-	-	-	-	-	-
			12 (CBCL)	64.15 (8.32)	65.83 (10.25)	Net Diff -4.6 (-9.2, -0.1)	-	-	-	-	-	-	-	-	-
			0 (PHYS)	18.52 (29.18)	32.76 (39.72)	-	-	-	-	-	-	-	-	-	-
			6 (PHYS)	62.22 (40.70)	75.17 (36.02)	Net Diff 1.3 (-18.2, 20.8)	-	-	-	-	-	-	-	-	-
			12 (PHYS)	75.24 (32.81)	56.95 (43.75)	Net Diff 32.5 (13.3, 51.8)	-	-	-	-	-	-	-	-	-

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
			0 (YHPS)	40.37 (36.64)	28.97 (35.29)	-	-	-	-	-	-	-	-	-	-
			6 (YHPS)	71.48 (39.00)	63.45 (44.18)	Net Diff -3.4 (-23.9, 17.2)	-	-	-	-	-	-	-	-	-
			12 (YHPS)	59.51 (41.04)	71.27 (35.61)	Net Diff -23.2 (-42.7, -3.6)	-	-	-	-	-	-	-	-	-
			0 (YSR)	69.03 (10.31)	68.55 (11.00)	-	-	-	-	-	-	-	-	-	-
			6 (YSR)	65.58 (9.91)	63.27 (6.53)	Net Diff 1.8 (-3.3, 7)	-	-	-	-	-	-	-	-	-
			12 (YSR)	60.19 (9.00)	60.67 (6.52)	Net Diff -1 (-6, 4.1)	-	-	-	-	-	-	-	-	-
Waldron 2001 [206, 207]	Fam (FFT) (N=30)	CBT + MI + Fam (N=29)	0	9.4 (3.8)	11.3 (4.1)	-	-	-	-	-	-	-	-	-	-
			4	8.2 (3.4)	9.1 (4.2)	Net Diff 1.0 (-0.8, 2.8)	-	-	-	-	-	-	-	-	-
			7	9.2 (3.8)	8.5 (4.2)	Net Diff 1.7 (-0.1, 3.5)	-	-	-	-	-	-	-	-	-
	Fam (FFT) (N=30)	CBT + MI (N=31)	0	9.4 (3.8)	11.3 (3.9)	-	-	-	-	-	-	-	-	-	-
			4	8.2 (3.4)	10.2 (3.8)	Net Diff -0.1 (-1.9, 1.7)	-	-	-	-	-	-	-	-	-

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
			7	9.2 (3.8)	10.4 (4.7)	Net Diff 0.7 (-1.1, 2.5)	-	-	-	-	-	-	-	-	-
	Fam (FFT) (N=30)	Educ +Peer Group (N=30)	0	9.4 (3.8)	10.3 (3.4)	-	-	-	-	-	-	-	-	-	-
			4	8.2 (3.4)	9.5 (3.5)	Net Diff -0.4 (-2, 1.2)	-	-	-	-	-	-	-	-	-
			7	9.2 (3.8)	9.4 (3.7)	Net Diff 0.7 (-0.9, 2.3)	-	-	-	-	-	-	-	-	-
	CBT + MI + Fam (N=29)	CBT + MI (N=31)	0	11.3 (4.1)	11.3 (3.9)	-	-	-	-	-	-	-	-	-	-
			4	9.1 (4.2)	10.2 (3.8)	Net Diff -1.1 (-3.1, 0.9)	-	-	-	-	-	-	-	-	-
			7	8.5 (4.2)	10.4 (4.7)	Net Diff -1.9 (-4.1, 0.3)	-	-	-	-	-	-	-	-	-
	CBT + MI + Fam (N=29)	Educ +Peer Group (N=30)	0	11.3 (4.1)	10.3 (3.4)	-	-	-	-	-	-	-	-	-	-
			4	9.1 (4.2)	9.5 (3.5)	Net Diff -1.4 (-3.4, 0.6)	-	-	-	-	-	-	-	-	-
			7	8.5 (4.2)	9.4 (3.7)	Net Diff -1.9 (-3.9, 0.1)	-	-	-	-	-	-	-	-	-

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
	CBT + MI (N=31)	Educ +Peer Group (N=30)	0	11.3 (3.9)	10.3 (3.4)	-	-	-	-	-	-	-	-	-	-
			4	10.2 (3.8)	9.5 (3.5)	Net Diff -0.3 (-2.1, 1.5)	-	-	-	-	-	-	-	-	-
			7	10.4 (4.7)	9.4 (3.7)	Net Diff 0.0 (-2.0, 2.0)	-	-	-	-	-	-	-	-	-
Schaeffer 2013 [185]	NOS + Apprentice training (N=50)	TAU (N=47)	0	25.78 (35.95)	28.32 (35.51)	-	1.90 (2.94)	3.17 (4.79)	-	2.24 (4.65)	5.0 (11.2)	-	-	-	-
			6	19.14 (32.36)	19.47 (36.11)	Net Diff 2.2 (-11.8, 16.2)	1.53 (2.46)	0.83 (1.86)	Net Diff 2.0 (0.6, 3.4)	2.35 (4.13)	2.03 (5.35)	Net Diff 3.1 (0, 6.1)	-	-	-
			12	11.11 (19.13)	12.49 (19.97)	Net Diff 1.2 (-11.2, 13.5)	1.29 (2.93)	1.26 (2.73)	Net Diff 1.3 (-0.1, 2.7)	0.71 (2.63)	1.60 (4.32)	Net Diff 1.9 (-1.1, 4.9)	-	-	-
			18	10.85 (22.18)	13.37 (24.46)	Net Diff 0 (-12.5, 12.5)	0.75 (1.41)	0.53 (1.22)	Net Diff 1.5 (0.1, 2.9)	0.80 (2.10)	0.77 (2.39)	Net Diff 2.8 (-0.3, 5.9)	-	-	-
			24	4.69 (7.91)	14.14 (25.27)	Net Diff -6.9 (-19.7, 5.9)	0.31 (0.89)	0.43 (0.98)	Net Diff 1.2 (-0.3, 2.6)	0.48 (1.88)	1.10 (3.49)	Net Diff 2.1 (-0.9, 5.2)	-	-	-
			30	1.61 (3.76)	4.87 (7.87)	Net Diff 0.7 (-14, 12.5)	0.33 (0.97)	0.47 (1.25)	Net Diff 1.1 (-0.3, 2.6)	0.11 (0.32)	0.80 (1.90)	Net Diff 2.1 (-1.1, 5.3)	-	-	-

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
Henggeler 2001 [129-133]	Fam (ecological) (N=58)	TAU (delivery group) (N=60)	0	62 (37)	59 (40)	-	-	-	-	-	-	-	-	-	-
			4	40 (39)	39 (36)	Net Diff -2.0 (-20.7, 16.7)	-	-	-	-	-	-	-	-	-
			11	32 (38)	30 (36)	Net Diff -1.0 (-19.6, 17.6)	-	-	-	-	-	-	-	-	-
			48	-	-	-	0.61 (0.90)	1.36 (2.21)	Mean Diff -0.75 (-1.48, 0.02)	0.89 (2.01)	1.26 (2.39)	Mean Diff -0.37 (-1.35, 0.61)	-	-	-
Henggeler 2006 [134]	Fam (drug court + multisytemic therapy + contingency) (N=37)	Fam (drug court + multisystemic therapy) (N=29)	0	-	-	-	4.2 (6.6)	6.9 (11.5)	-	4.4 (6.4)	6.2 (9.8)	-	13.9 (22.6)	15.4 (23.2)	-
			4	-	-	-	7.2 (21.0)	3.2 (4.2)	Net Diff 6.7 (-0.3, 13.7)	1.8 (3.0)	1.6 (5.2)	Net Diff 2.0 (-1.6, 5.7)	8.2 (19.0)	3.5 (4.7)	Net Diff 6.2 (-4.1, 16.5)
			12	-	-	-	1.8 (4.5)	2.8 (8.3)	Net Diff 1.7 (-2.5, 5. 9)	1.2 (2.5)	1.0 (4.5)	Net Diff 2.0 (-1.6, 5.6)	3.5 (6.4)	2.6 (5.8)	Net Diff 2.4 (-7.6, 12.4)

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
	Fam (drug court + multisytemic therapy + contingency) (N=37)	TAU (family court + community services) (N=32)	0	-	-	-	4.2 (6.6)	9.5 (17.5)	-	4.4 (6.4)	8.9 (13.7)	-	13.9 (22.6)	7.8 (6.3)	-
			4	-	-	-	7.2 (21.0)	3.0 (5.5)	Net Diff 9.5 (1.27, 17.73)	1.8 (3.0)	2.7 (5.4)	Net Diff 3.6 (-0.9, 8.1)	8.2 (19.0)	6.9 (11.0)	Net Diff -4.8 (-12.34, 2.74)
			12	-	-	-	1.8 (4.5)	10.7 (28.2)	Net Diff -3.6 (-12.77, 5.57)	1.2 (2.5)	2.5 (5.7)	Net Diff 3.2 (-1.3, 7.7)	3.5 (6.4)	16.8 (38.8)	Net Diff -19.4 (-33.5, -5.3)
	Fam (drug court + multisytemic therapy + contingency) (N=37)	TAU (drug court + community services) (N=29)	0	-	-	-	4.2 (6.6)	3.7 (4.9)	-	4.4 (6.4)	5.2 (9.8)	-	13.9 (22.6)	8.6 (10.6)	-
			4	-	-	-	7.2 (21.0)	2.3 (4.6)	Net Diff 4.4 (-1.84, 10.64)	1.8 (3.0)	2.3 (5.2)	Net Diff 0.3 (-3.3, 3.9)	8.2 (19.0)	4.4 (7.4)	Net Diff -1.5 (-9.1, 6.1)
			12	-	-	-	1.8 (4.5)	1.0 (2.2)	Net Diff 0.3 (-2.1, 2.7)	1.2 (2.5)	1.9 (7.2)	Net Diff 0.1 (-3.5, 3.7)	3.5 (6.4)	1.4 (2.4)	Net Diff -3.2 (-10.59, 4.19)

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
	Fam (drug court + multisystemic therapy) (N=29)	TAU (family court + community services) (N=32)	0	-	-	-	6.9 (11.5)	9.5 (17.5)	-	6.2 (9.8)	8.9 (13.7)	-	15.4 (23.2)	7.8 (6.3)	-
			4	-	-	-	3.2 (4.2)	3.0 (5.5)	Net Diff 2.8 (-3.7, 9.3)	1.6 (5.2)	2.7 (5.4)	Net Diff 2.0 (-3.2, 7.2)	3.5 (4.7)	6.9 (11.0)	Net Diff -11 (-19.4, -2.6)
			12	-	-	-	2.8 (8.3)	10.7 (28.2)	Net Diff -5.3 (-14.6, 4.0)	1.0 (4.5)	2.5 (5.7)	Net Diff 1.2 (-4, 6.4)	2.6 (5.8)	16.8 (38.8)	Net Diff -21.8 (-36.4, -7.2)
	Fam (drug court + multisystemic therapy) (N=29)	TAU (drug court + community services) (N=29)	0	-	-	-	6.9 (11.5)	3.7 (4.9)	-	6.2 (9.8)	5.2 (9.8)	-	15.4 (23.2)	8.6 (10.6)	-
			4	-	-	-	3.2 (4.2)	2.3 (4.6)	Net Diff -2.3 (-6.4, 1.8)	1.6 (5.2)	2.3 (5.2)	Net Diff -1.7 (-6.1, 2.7)	3.5 (4.7)	4.4 (7.4)	Net Diff -7.7 (-16.2, 0.8)
			12	-	-	-	2.8 (8.3)	1.0 (2.2)	Net Diff -1.4 (-5.4, 2.6)	1.0 (4.5)	1.9 (7.2)	Net Diff -1.9 (-6.4, 2.6)	2.6 (5.8)	1.4 (2.4)	Net Diff -5.6 (-14, 2.8)
	TAU (family court + community services) (N=32)	TAU (drug court + community services) (N=29)	0	-	-	-	9.5 (17.5)	3.7 (4.9)	-	8.9 (13.7)	5.2 (9.8)	-	7.8 (6.3)	8.6 (10.6)	-

Author (Year) PMID	Arm 1	Arm 2	Time (Months)	General Del. Int.	General Del. Cont.	General Del. Calc. Effect (95% CI)	Person Crimes Int.	Person Crimes Cont.	Person Crimes Calc. Effect (95% CI)	Property Crimes/ Theft Int.	Property Crimes/ Theft Cont.	Property Crimes/ Theft Calc. Effect (95% CI)	Status Offense Int.	Status Offense Cont.	Status Offense Calc. Effect (95% CI)
			4	-	-	-	3.0 (5.5)	2.3 (4.6)	Net Diff -5.1 (-10.7, 0.5)	2.7 (5.4)	2.3 (5.2)	Net Diff -3.3 (-8.5, 1.9)	6.9 (11.0)	4.4 (7.4)	Net Diff 3.3 (-1.5, 8.1)
			12	-	-	-	10.7 (28.2)	1.0 (2.2)	Net Diff 3.9 (-4.8, 12.6)	2.5 (5.7)	1.9 (7.2)	Net Diff -3.1 (-8.3, 2.1)	16.8 (38.8)	1.4 (2.4)	Net Diff 16.2 (3.2, 29.2)

Appendix H. Risk of Bias Assessments

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention to Treat Analysis	Group Similarity at Baseline	Co-Interventions	Compliance	Timing of Outcome Assessments	Additional Bias
Amini, 1982 CN-00182281 (Cochrane)	U	U	H	H	U	L	U	H	L	L	U	L	No
Arnaud, 2015 2016-03749-004 (psycINFO)	L	L	H	U	H	H	U	H	L	L	H	L	No
Arnaud, 2017 27801991	U	U	H	H	U	L	U	L	H	L	U	L	No
Azrin, 1994 CN-00241903 (Cochrane)	H	U	H	H	U	L	U	H	L	L	L	L	No
Azrin, 2001 2002-13926-001 (psycINFO)	L	U	H	H	L	H	U	H	H	H	H	H	No
Baer, 2007 18072842	L	U	H	H	U	H	U	H	L	L	H	L	No
Bernstein, 2009 20053238	L	L	H	H	L	H	U	H	L	L	U	L	No
Bernstein, 2010 20670329	L	L	H	H	L	H	U	H	L	L	U	L	No
Braciszewski, 2018 132804409 (embase)	H		H	H	H	H	U	L	L	L	L	L	No
Brown, 2015 26362000	U	U	H	H	L	H	U	H	L	L	L	L	No
Burrow-Sanchez, 2012 22866693	U	U	H	H	U	H	U	L	U	L	L	L	No
Burrow-Sanchez, 2015 25602465	L	L	L	H	L	L	U	L	L	L	H	L	No
Colby, 2018 29750362	L	U	H	H	L	L	U	L	H	L	U	L	No
Cornelius, 2009 19321268	L	L	L	L	L	L	U	L	H	H	U	L	No
Cornelius, 2010 20576364	L	U	L	L	L	L	U	L	L	L	U	L	No
Cunningham, 2015 26347440	L	U	H	H	U	L	U	L	L	L	L	L	No

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention to Treat Analysis	Group Similarity at Baseline	Co-Interventions	Compliance	Timing of Outcome Assessments	Additional Bias
D'Amico, 2008 18037603	U	U	H	H	H	H	U	H	U	L	U	H	No
D'Amico, 2013 CN-00917707 (Cochrane)	U	U	H	H	U	L	U	H	H	L	L	L	No
D'Amico, 2018 30138016	L	U	H	H	H	L	U	L	L	L	H	L	No
Dakof, 2015 25621927	L	U	H	H	U	H	U	L	L	L	H	L	No
de Gee, 2014 24969735	L	U	H	H	H	H	L	L	L	H	L	L	No
De Sousa, 2008 CN-00753784 (Cochrane)	L	H	H	H	H	L	U	L	L	L	L	L	No
De Sousa, 2014 CN-01014147 (Cochrane)	L	H	H	H	H	L	U	L	L	L	L	L	No
Delbelo, 2017 NCT00550394 (ctg)	U	U	L	L	L	H	U	H	U	L	U	L	No
Delbelo, 2017 NCT00393978 (ctg)	L	U	L	L	L	H	U	L	U	L	U	L	No
Dembo, 2014 2014-42452-005 (psycINFO)	U	U	H	H	U	L	U	U	U	L	L	L	No
Dennis, 2004 15501373 (trial 1)	L	L	H	H	L	L	U	L	L	L	U	L	No
Dennis, 2004 15501373 (trial 2)	L	L	H	H	L	L	U	L	L	L	U	L	No
Esposito-Smythers, 2011 22004303	L	L	H	H	L	L	U	H	L	L	H	L	No
Figurelli, 1994 7862806	U	U	H	H	U	L	U	L	U	L	L	L	No
Findling, 2009 19298659	L	L	L	H	L	H	U	L	L	L	H	L	No
Friedman, 1989 CN-00496580 (Cochrane)	U	U	H	H	H	H	U	H	H	L	H	H	Yes: Parents of older children less participatory (thus excluded).
Geller, 1998 9473913	U	U	L	L	L	L	U	L	L	L	L	L	No
Giles, 2019 CN-01953820 (cochrane)	L	H	H	H	H	L	U	L	L	L	L	L	No

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention to Treat Analysis	Group Similarity at Baseline	Co-Interventions	Compliance	Timing of Outcome Assessments	Additional Bias
Godley, 2002 12127465	L	L	H	H	L	L	U	L	L	L	H	L	No
Godley, 2010 20219293	L	H	H	H	L	L	U	L	L	L	U	L	No
Godley, 2019 CN-01745749 (Cochrane)	L	U	H	H	L	L	U	L	L	L	L	L	No
Gonzalez, 2015 26454835	L	U	L	L	L	H	U	L	L	L	L	L	No
Gray, 2012 22706327	U	U	L	L	L	L	U	L	L	H	H	H	No
Henderson, 2016 26992083	L	L	H	H	U	L	U	L	L	L	U	L	No
Henggeler, 1996 8610836	U	U	H	H	U	L	U	U		L	U	L	No
Henggeler, 2006 16551142	L	L	H	H	U	L	U	L	H	L	U	L	No
Henggeler, 2012 22309470	U	U	H	H	H	L	U	L	L	L	L	U	Yes: 2 judicial courts randomized to "usual services" lost funding and were replaced with 2 others.
HJoanning, 1992 CN-00631575 (Cochrane)	H	H	H	H	H	H	U	H	L	L	L	L	Yes: 1. Family members of those in AGT arm were substantially less willing to participate (or have children participate) than other groups. 2. Drug use estimates relied largely on adult perceptions of overall youth behavior.
Hogue, 2015 25496283	L	U	H	H	U	L	U	L	L	L	H	L	No
Kaminer, 1998 9824170	U	U	H	H	L	H	U	U	L	L	H	L	No
Kaminer, 2002 12436013	U	U	H	H	U	H	U	U	L	L	H	L	No
Kaminer, 2008 18978635	L	U	H	H	U	L	U	L	L	L	L	L	No

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention to Treat Analysis	Group Similarity at Baseline	Co-Interventions	Compliance	Timing of Outcome Assessments	Additional Bias
Kelly, 2017 28742932	U	U	L	H	H	H	U	L	L	L	L	L	No
Killeen, 2012 22299805	U	U	H	U	U	H	U	L	L	L	H	L	No
Latimer, 2003 12957348	U	U	H	H	U	L	U	L	L	L	U	L	No
Letourneau, 2017 27629581	U	U	H	H	H	L	U	L	L	L	L	L	No
Liddle, 2001 11727882	U	U	H	H	L	U	U	U	H	L	H	L	No
Liddle, 2004 15152709	L	U	H	H	L	L	U	L	L	L	H	L	No
Liddle, 2008 18705691	U	L	H	H	L	H	U	L	L	L	U	L	No
Liddle, 2018 29866383	L	U	H	H	H	L	U	L	L	L	H	L	No
Lowe, 2012 22931079	U	U	H	H	H	U	U	U	L	L	U	L	No
Marsch, 2005 16203961	U	U	L	L	L	U	U	L	L	L	H	L	No
Marsch, 2016 26918564	U	U	L	L	L	H	U	L	H	L	H	L	No
Marsden, 2006 16771893	U	L	H	H	H	L	U	L	H	L	L	L	No
Martin, 2008 17869051	L	L	H	H	H	L	U	L	L	H	L	L	No
Martínez Martínez, 2008 2009-05582-007 (psycINFO)	U	U	H	H	H	H	U	H	U	H	L	L	No
Mason, 2015 26234955	L	U	H	H	H	L	U	L	L	L	L	L	No
McCambridge, 2004 14678061	H	L	H	H	H	L	U	L	H	L	L	L	No
McCambridge, 2008 18778385	L	L	H	H	H	L	U	L	L	L	U	L	No
McCarty, 2019 30883284	L	U	H	H	H	L	U	H	L	L	L	L	No
Miranda, 2014 23489253	U	U	L	L	L	H	U	H	L	L	L	L	No
Miranda, 2017 26752416	L	U	L	L	L	H	U	H	L	H	H	L	No
Monti, 1999 10596521	U	U	H	H	H	L	U	L	L	L	L	L	No

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention to Treat Analysis	Group Similarity at Baseline	Co-Interventions	Compliance	Timing of Outcome Assessments	Additional Bias
Najavits, 2006 16858633	U	L	H	H	H		H	L	L	L	L	L	No
Niederhofer, 2003 15385223	U	L	L	L	L	H	U	H	L	L	H	L	No
Niederhofer, 2003 12554608	U	U	L	L	L	H	U	H		L	U	L	No
Niederhofer, 2003 CN-00474316 (Cochrane)	L	U	L	L	L	L	U	L	U	H	L	L	No
O'Malley, 2015 25742208	U	L	L	L	L	L	U	H	L	L	L	L	No
Ogel, 2011 21609157	U	H	H	H	H	H	U	H	L	L	L	L	No
Peterson, 2006 16938063	L	L	H	H	H	L	U	L	L	L	L	L	No
Riggs, 2004 15187802	U	L	L	L	L	H	U	L	H	L	U	L	No
Riggs, 2007 17984403	U	L	L	L	L	L	U	L	L	L	L	L	No
Riggs, 2011 21871372	U	L	L	L	L	H	U	L	L	L	L	L	No
Rigter, 2013 23140805	U	L	H	H	L	L	U	L	L	L	H	L	No
Robbins, 2008 18266532	L	U	H	H	L	L	U	L	U	H	L	L	No
Robbins, 2011 21967492	L	L	H	H	L	H	U	L	L	L	H	L	No
Rohde, 2014 24491069	U	U	H	H	U	L	U	H	L	L	U	L	No
Rowe, 2016 26879671	L	U	H	H	L	L	U	L	U	L	L	L	No
Santisteban, 2011 21639636	U	U	H	H	L	L	U	H	H	L	L	L	Yes: NA
Santisteban, 2015 25799306	U	U	H	H	H	L	U	H	L	L	U	L	No
Schaeffer, 2014 23958035	L	L	H	H	U	H	U	L	L	L	U	L	No
Slesnick, 2005 15878048	L	U	H	H	U	H	U	H	L	L	H	L	No
Slesnick, 2007 16989957	L	L	H	H	H	H	U	L	L	L	L	L	No

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention to Treat Analysis	Group Similarity at Baseline	Co-Interventions	Compliance	Timing of Outcome Assessments	Additional Bias
Slesnick, 2009 19522781	L	U	H	H	U	U	U	H	H	L	H	L	No
Slesnick, 2013 23895088	L	U	H	H	U	H	U	L	L	L	H	L	No
Slesnick, 2015 25736623	L	U	H	H	U	H	U	L	L	L	H	L	No
Smith, 2006 17182429	U	U	H	H	U	L	U	L	U	U	H	L	No
Smith, 2015 25551562	U	L	H	H	L	L	U	L	L	L	H	L	No
Spijkerman, 2010 21169172	L	L	H	U	H	L	U	L	L	L	L	L	No
Spirito, 2004 15343198	L	U	H	H	L	L	U	U	L	L	L	L	No
Spirito, 2011 21383276	U	L	H	H	L	L	U	H	L	L	H	L	No
Spirito, 2017 29252011	L	L	H	H	H	L	U	L	L	L	L	L	No
Srisurapanont, 2007 17453612	L	L	H	H	H	H	U	H	L	L	L	L	No
Stanger, 2009 19717250	L	U	H	H	H	H	U	L	L	L	H	L	No
Stanger, 2015 26004659	U	U	H	H	H	H	U	L	L	L	L	L	No
Stanger, 2017 28414474	U	U	H	H	H	H	U	H	L	L	U	L	No
Stein, 2011 21531089	L	L	H	H	L	L	U	U	L	L	U	L	No
Tait, 2004 15194207	L	L	H	H	H	H	U	L	L	L	L	L	No
Thurstone, 2010 20494267	U	L	L	L	L	L	U	L	H	L	L	L	No
Thush, 2007 16928395	U	U	H	H	H	L	U	U	U	L	U	L	No
Tolou-Shams, 2017 CN-01365355 (Cochrane)	U	U	H	H	H	L	U	H	H	L	H	L	No

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention to Treat Analysis	Group Similarity at Baseline	Co-Interventions	Compliance	Timing of Outcome Assessments	Additional Bias
Trudeau, 2017 2017-00657-001 (psycINFO)	L	L	H	H	H	L	U	H	L	L	U	L	Yes: Unexplained large difference in numbers randomized to each group. Changed randomization method after start (although, they said "re-randomized).
Voogt, 2013 CN-01122318 (Cochrane)	L	L	H	H	U	H	U	L	L	L	U	L	No
Wagner, 2014 24841864	L	U	H	H	L	H	U	L	L	L	L	L	No
Waldron, 2001 11680557	L	U	H	H	U	L	U	H	L	L	L	L	No
Walker, 2006 16822119	U	U	H	H	U	L	U	H	U	L	U	L	No
Walker, 2011 21688877	L	L	H	H	H	L	U		L	L	L	L	No
Walker, 2016 27762569	U	U	H	H	H	H	U	L	L	L	L	L	No
Winters, 2007 17563146	U	U	H	H	L	L	U	H	L	L	L	L	No
Winters, 2012 22000326	U	U	H	H	L	L	U	L	L	L	L	L	Yes: The assessment-only control group was recruited later than the two intervention groups. Recruitment cut short, resulting in TAU being 1/2 the N of intervention arms.
Woody, 2008 18984887	L	L	H	H	H	H	U	L	L	H	H	L	No
Zhang, 2018 30556713	L	U	H	H	H	H	U	L	L	L	L	L	No

Random sequence generation (selection bias): Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence; Allocation concealment (selection bias): Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment; Blinding of participants (performance bias): Performance bias due to knowledge of the allocated interventions by participants during the study; Blinding of personnel/ care providers (performance bias): Performance bias due to knowledge of the allocated interventions by personnel/care providers during the study; Blinding of

outcome assessor (detection bias): Detection bias due to knowledge of the allocated interventions by outcome assessors; Incomplete outcome data (attrition bias): Attrition bias due to amount, nature or handling of incomplete outcome data; Intention-to-treat-analysis: Bias due to incomplete reporting and analysis according to group allocation; Group similarity at baseline (selection bias): Selection bias due to dissimilarity at baseline for the most important prognostic indicators; Co-interventions (performance bias): Performance bias because co-interventions were different across groups; Compliance (performance bias): Performance bias due to inappropriate compliance with interventions across groups; Timing of outcome assessments (detection bias): Detection bias because important outcomes were not measured at the same time across groups; Additional Bias: Bias due to problems not covered elsewhere in the table; Abbreviations: H=high risk of bias; U = unclear risk of bias; L = low risk of bias

Appendix I. Technical Appendix

TA Trikalinos, DW Steele

Network Meta-analysis Models

We provide a detailed description of the models used in the main analysis.

Notation

Let $k = 1, \dots, K$ index studies and $(j = 1, \dots, J)$ index treatments in a network meta-analysis. For *continuous outcomes*, write x_{kj} for the mean and σ_{kj}^2 for the conditional (sampling) variance of the responses with treatment j in trial k.[1]

For *dichotomous outcomes*, write r_{kj} for the number of people with events and N_{kj} for the total number of people who received treatment j in trial k.

Encode what treatment was assigned in an arm in a trial using the $(J-1)$-long row vector

$$\mathbf{T}_{kj} = \begin{cases} (0, \dots, 1_{[j]}, \dots, 0) & \text{if } j < J \\ (0, \dots, 0) & \text{if } j = J \end{cases}. \qquad (1)$$

where has $1_{[j]}$ means '1 at the j-th position'. This can be used as a row in a design matrix encoded such that treatment J is the reference treatment.

Model

Network meta-analysis is mathematically equivalent to a 2-level hierarchical model.

Observational Part

The first level (observational part) models the conditional distribution of data within each trial. For continuous outcomes, write:

$$x_{kj} \sim N(\mu_{kj}, \sigma_{kj}^2) \qquad (2)$$
$$\mu_{kj} = \mathbf{T}_{kj}\boldsymbol{\delta}_k + \alpha_k, \qquad (3)$$

where $\boldsymbol{\delta}_k = (\delta_{k1}, \dots, \delta_{k,J-1})'$ is a column vector of basic parameters, α_k is a study-specific intercept, and $'$ denotes transpose. The α_k can be interpreted as the mean of the

[1] If trial k compares a strict subset of the J treatments, say j_1, j_2, and j_3, $j \in \{j_1, j_2, j_3\} = \mathcal{J}_k \subset \{1,2,\dots,J\} = \mathcal{J}$.

outcome under treatment j. Each δ_{kj} can be interpreted as the difference in the mean of the outcome between treatment $j < J$ and treatment J in study k.

For dichotomous outcomes (2) and (3) become:

$$\begin{aligned} r_{kj} &\sim \text{Bin}(\pi_{kj}, N_{kj}) && (4)\\ \mu_{kj} &:= \text{logit}(\pi_{kj}) && (5)\\ &= \mathbf{T}_{kj}\boldsymbol{\delta}_k + \alpha_k, && (6) \end{aligned}$$

where now the α_k can be interpreted as the log-odds of the probability of the outcome under treatment J. Each δ_{kj} can be interpreted as the difference in the log-odds of the probability of the outcome between treatment $j < J$ and treatment J in study k.

The model in (3) (or in (6) for dichotomous outcomes) explicitly encodes a *consistency* assumption between direct and indirect effects.[2]

Structural Part

The structural part of the model prescribes how the study-specific parameters are related.

The Intercepts α_k

We modeled the intercepts as fixed constants.

The Treatment Effects $\boldsymbol{\delta}_k$

We considered two variants.

1. Under an *equal effect* model

$$\boldsymbol{\delta}_k = \boldsymbol{\delta},$$

2. for all k. In this case the hierarchical model degenerates to a heteroskedastic regression model.

3. Under a *random effects* model, treatment-specific effects are modeled with a multivariate normal distribution

$$\boldsymbol{\delta}_k \sim N(\boldsymbol{\delta}, \boldsymbol{\Sigma}),$$

[2] Model (3) reduces the number of treatment effects in the network's graph from $|\mathcal{E}| \geq J - 1$ to the $J - 1$ in $\boldsymbol{\delta}_k$. All other effects are recovered as convex combinations of the elements of $\boldsymbol{\delta}_k$.

4. where $\boldsymbol{\delta} = (\delta_1, \ldots, \delta_{J-1})'$ is a column vector of between-study means and covariance matrix

$$\boldsymbol{\Sigma} = \tau^2 \boldsymbol{\Omega}.$$

5. In (9), $\boldsymbol{\Omega}$ is a square correlation matrix. τ^2 is a between-study variance parameter which we assume to be the same for all treatment effects. This *homogeneity of variances* assumption is commonly employed. The homogeneity of variances assumption together with (3) or (6) imply that $\boldsymbol{\Omega}$ has a compound-symmetry structure with all off-diagonal elements equal to 0.5 and all diagonal elements equal to 1.[3]

Comparison of Direct and Indirect Estimates of an Effect

Consider a network with $J + 1$ treatments, where treatment j in the set of studies that include a comparison of interest (say, j vs. i) is considered as j^*. Implementing the models previously described, the direct estimate for the comparison of interest is then the contrast between treatment j^* and treatment i, and the indirect estimate is the contrast between treatment j and treatment i. The consistency factor is then the contrast between treatment j^* and j.

Computation

We fit models with *gemtc*, which uses *rjags* in R and JAGS for the Bayesian computation. Graph operations were done with *igraph* in R.

[3] To show, start from (3) (equivalently, from (6) for dichotomous outcomes) and take variances.